Thesis for doctoral degree (Ph.D.) 2016

MENTAL DISORDERS AND VIOLENCE RISK; EPIDEMIOLOGICAL AND CLINICAL COHORT STUDIES

Tomas Moberg

Karolinska Institutet

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Stockholm 2016

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Published by Karolinska Institutet.
Printed by Eprint AB 2015

ISBN 978-91-7676-185-4

MENTAL DISORDERS AND VIOLENCE RISK; EPIDEMIOLOGICAL AND CLINICAL COHORT STUDIES

THESIS FOR DOCTORAL DEGREE (Ph.D.)

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To Cecilia

ABSTRACT

Introduction

Violence morbidity and mortality has been increasingly recognized to be of importance for public health. The relationship between mental illness and violent crime is complex because of the involvement of several confounding risk factors.

Aim

The aim of this thesis was to study the risk of interpersonal violence and violent crime in common mental disorders with a focus on the effect of early risk factors, the relationship between interpersonal violence and the serotonin system, as well as the risk of death.

Methods

A birth cohort of 49,000 Swedish men was followed longitudinally in registers for 35 years after conscription and two clinical cohorts of 42 and 161 suicide attempters, respectively, were studied using cross-sectional study designs. Interpersonal violence was studied among individuals with a mental disorder using group comparisons, correlation analyses, and relative risks measured by means of odds ratios and confidence intervals from bivariate and multivariate logistic regression. Mortality was studied among violent offenders using Cox proportional hazard regression analyses.

Results

Mental disorders led to a general increase in the risk for interpersonal violence and violent recidivists had a higher mortality. Mental Retardation, Substance-Related Disorders and early behavioural problems, including violent behaviour in childhood, were important predictors of expressed interpersonal violence in adults. Personality Disorders were a predictor of expressed interpersonal violence in men. Affective-Anxiety Disorders were weak predictors of adult interpersonal violence. No association was found between Psychosis and violent offending. Childhood maltreatment was shown to be a weak predictor of adult interpersonal violence, with aggression dyscontrol only in a subgroup of traumatized individuals with low levels of a serotonin metabolite in the cerebrospinal fluid. Violent recidivists had a significantly higher risk of dying from an Alcohol- or Drug-Related Disorder and by suicide.

Conclusions

Violence risk assessments should include a thorough psychiatric and psychological evaluation, including cognitive tests and information about early behavioural problems and childhood maltreatment. Mental Retardation should be included in the violence risk assessment instruments. Risk assessments for violence also provide tools to identify violent offenders who are at high risk of mortality.

LIST OF SCIENTIFIC PAPERS

I. **Moberg T**, Stenbacka M, Tengström A, Jönsson EG, Nordström P, Jokinen J: Psychiatric and neurological disorders in late adolescence and risk of convictions for violent crime in men. *BMC Psychiatry* 2015, 15(1):299.

II. **Moberg T**, Stenbacka M, Jönsson EG, Nordström P, Åsberg M, Jokinen J: Risk factors for adult interpersonal violence in suicide attempters. *BMC Psychiatry* 2014, 14:195.

III. **Moberg T**, Nordström P, Forslund K, Kristiansson M, Åsberg M, Jokinen J: CSF 5-HIAA and exposure to and expression of interpersonal violence in suicide attempters. *Journal of Affective Disorders* 2011, 132(1-2):173-178.

IV. Stenbacka M, **Moberg T**, Romelsjö A, Jokinen J: Mortality and causes of death among violent offenders and victims – a Swedish population-based longitudinal study. *BMC Public Health* 2012, 12:38.

CONTENTS

LIST OF ABBREVIATIONS

5-HIAA	5-hydroxyindoleacetic acid, serotonin metabolite
5-HT	5-hydroxytryptamine, serotonin
ASPD	Antisocial Personality Disorder
AUC	Area under the curve
BPD	Borderline Personality Disorder
CI	Confidence interval
CSF	Cerebrospinal fluid
DSM-III-R	The Diagnostic and Statistical Manual of Mental Disorders, Third Revised Edition
DSM-IV	The Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition
EEQ	Early Experience Questionnaire
GC-MS	Gas chromatography–Mass spectrometry
HCR-20^{V3}	Historical-Clinical-Risk Management-20, Version 3
HDHQ	Hostility and Direction of Hostility Questionnaire
HR	Hazard ratio
ICD	International Classification of Diseases
IPV	Intimate partner violence
LSI-R	Level of Service Inventory – Revised
MADRS	Montgomery–Åsberg Depression Rating Scale

MAOA	Monoamine oxidase A, neurotransmitter-metabolizingenzyme
KIVS	Karolinska Interpersonal Violence Scale
OR	Odds ratio
PCL-R	Psychopathy Checklist – Revised
PET	Positron emission tomography
ROC	Receiver operating characteristic
SARA: SV	Spousal Assault Risk Assessment: Short Version
SCID	Structured Clinical Interview for DSM-III-R or DSM-IV, Axis I (SCID I) and Axis II (SCID II)
SD	Standard deviation
V-RISK-10	Violence Risk Screening-10
WHO	World Health Organization

1 INTRODUCTION

1.1 MENTAL DISORDERS

The main focus of this thesis was to study common mental disorders, also known as psychiatric disorders, and associated risks for violence. The psychiatric conditions studied in Study I were Psychoses, Anxiety-Depression/neuroses, Personality Disorders, Substance-Related Disorders and Mental Retardation diagnosed during clinical interviews in accord with the International Classification of Diseases, Revision 8 (ICD-8) [1]. A sixth diagnostic group, Neurological and other central nervous system conditions, was also studied although the diagnoses in this group are not classified as mental disorders. In Studies II and III, the diagnoses of interest were Mood-Anxiety diagnoses, Personality Disorders and Substance-Related Disorders. The diagnoses were confirmed according to the Diagnostic and Statistical Manual of Mental Disorders, Third Revised (DSM-III-R) and Fourth Editions (DSM-IV) using two semi-structured clinical interviews [2-5]. In Study IV the same mental disorders as in Study I were of interest, but the diagnostic systems used also included ICD-9 and ICD-10 [6, 7].

1.2 VIOLENCE

The importance of violence morbidity and mortality for public health has been increasingly recognized and the World Health Organization (WHO) has estimated that more than 0.5 million people lost their lives because of homicide in the year 2000 alone [8].

Aggression and violence are classified as either premeditated or impulsive. Premeditated violence constitutes a planned behaviour, which is not typically associated with frustration or response to an immediate threat and is planned with clear goals in mind. Impulsive violence is associated with negative emotions such as anger or fear and is usually a response to a perceived stress [9].

A definition of violence was developed by a WHO working group in 1996: “The intentional use of physical force or power, threatened or actual, against oneself, another person, or against a group or community, that either results in or has a high likelihood of resulting in injury, death, psychological harm, maldevelopment or deprivation” [10]. Violence is divided into three broad categories: self-inflicted, interpersonal, and collective (Figure 1). Each category is subdivided to reflect specific types of violence, settings of violence, and nature of violent acts: physical, sexual, psychological and deprivation or neglect [11]. The focus in the studies in this thesis was on studying physical interpersonal violence among adult men in Studies I and IV and on physical or sexual interpersonal violence among adult suicide attempters in Studies II and III.

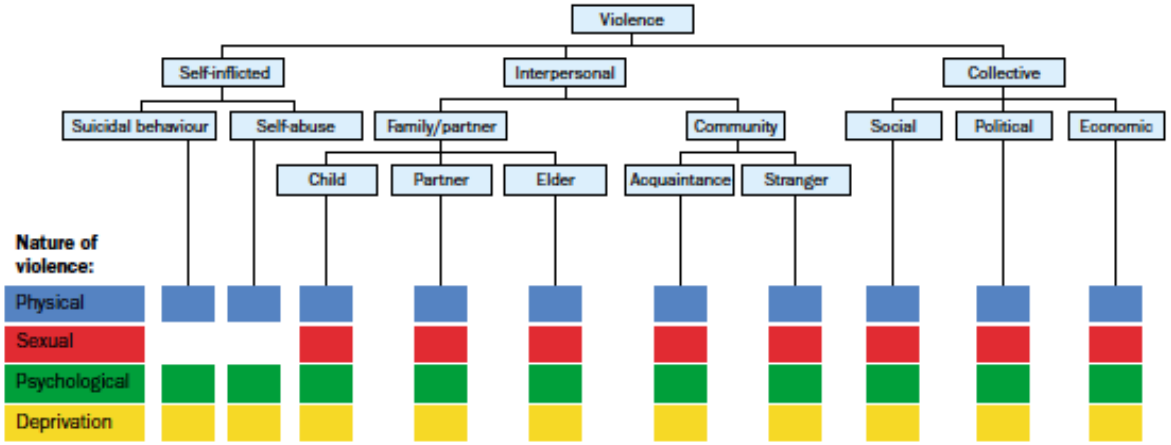

Figure 1. Types of violence.

1.3 VIOLENCE RISK ASSESSMENT INSTRUMENTS

Violence risk assessment has been the subject of considerable clinical and research interest. The purpose of doing violence risk assessments in clinical settings is to reduce the risk of interpersonal violence by identifying the factors that increase the risk of violence and then offering support or treatment for those factors. More than 100 risk assessment tools have been developed and are used increasingly in clinical and criminal justice settings. The group of risk assessment tools is often divided into actuarial instruments, which provide a probabilistic estimate of violence risk in a specified time period, and structured clinical judgment instruments for making a professional judgment on the violence risk level (for example, low, moderate or high) after taking into account the presence or absence of a predetermined set of factors. There is considerable uncertainty about how these tools should be used and for whom [12]. Frequently used actuarial instruments include the Level of Service Inventory – Revised (LSI-R) [13] and the Psychopathy Checklist – Revised (PCL-R) [14]. Frequently used structured clinical judgment tools include the Historical-Clinical-Risk Management-20, Version 3 ($HCR\text{-}20^{V3}$) [15], the Spousal Assault Risk Assessment: Short Version (SARA: SV) [16] and the Violence Risk Screening-10 (V-RISK-10) [17]. The risk assessment instruments include items assessing different psychiatric disorders or symptoms.

1.4 PSYCHOTIC DISORDER AS A POTENTIAL RISK FACTOR FOR THE USE OF VIOLENCE

The significance of Psychotic Disorders for severe violent crimes has been studied and this diagnostic group was apparently over-represented in a well-characterized cohort of homicide offenders [18], as well as in studies on other violent crimes [19-22]. The use of antipsychotics in patients with Schizophrenia, as well as in other groups of psychiatric patients, has been shown to reduce the violence risk [23]. Other factors such as Substance Use Disorders have been suggested to be a possible mediator for the increase in the risk of violent crime among patients with Psychoses [24, 25].

1.5 AFFECTIVE DISORDER AS A POTENTIAL RISK FACTOR FOR THE USE OF VIOLENCE

It has been the subject of controversy whether or not Affective Disorders *per se* contribute to the increased risk of violent crime or if the elevated risk of violence reported among subjects with these disorders in some studies is caused by a confounding effect. Several studies have failed to demonstrate a statistically significant relationship between Affective Disorders and violent crime, when co-morbid conditions such as Substance Abuse have been taking into account. [25, 26]. Other studies have suggested instead that there is a statistically significant, yet modest, relationship with violence not explained by confounders [27], particularly for Bipolar Disorder [28-30].

1.6 PERSONALITY DISORDER AS A POTENTIAL RISK FACTOR FOR THE USE OF VIOLENCE

Personality Disorders and Substance Use Disorders are the psychiatric conditions suggested to increase the risk of recurrence of violent crimes the most [31]. Antisocial Personality Disorder (ASPD) and Borderline Personality Disorder (BPD), in particular, are considered to enhance the risk of violence [32], but violent behaviours, either directly or indirectly, constitute part of the operational criteria for these diagnoses and therefore suggest caution in the interpretation of the literature [33]. Psychopathy is more like a personality trait and is not classified as a Personality Disorder, but it is a substantial risk factor for violence [34]. Even though ASPD and Psychopathy are different constructs, it has been suggested that ASPD is on a continuum with Psychopathy [35] and both appear to be mediators of violence in patients with BPD [36-38], which diminishes the independent predictive effect of BPD on violence.

1.7 SUBSTANCE-RELATED DISORDER AS A POTENTIAL RISK FACTOR FOR THE USE OF VIOLENCE

Alcoholism and Drug Dependence are well-established risk factors for violence [39]. The relation between acute alcohol or drug consumption and aggressive behaviour is a complex phenomenon that has been studied in a variety of different disciplines. The aim for many studies has been to evaluate the extent to which other factors that co-vary with substance use problems could add above and beyond the risk ratios found for Substance Use Disorders when it comes to understanding violent offending [31, 40]. Among these suggested factors for an increased risk of violence in connection with Substance Use Disorders are antisocial traits and behaviour [41] and a propensity to react with aggression in conflicts [42]. It has been suggested that impulsivity may be a dimension of psychopathology representing dysfunctional reward processing and ultimately resulting in compulsive behaviours ranging from drug addiction to impulsive violence [43].

1.8 MENTAL RETARDATION AS A POTENTIAL RISK FACTOR FOR THE USE OF VIOLENCE

The impact of Mental Retardation on violent offending has been demonstrated in studies on inmates in the criminal justice system, where the prevalence of Mental Retardation has been reported to vary from 2% up to 40%, the wide range being due to methodological factors [44]. Mental Retardation was found to be an important risk factor for violent offending in an early longitudinal study [45], a result which, to some extent, has subsequently been disputed [46]. Even though Mental Retardation may be over-represented in parts of the criminal justice system [47], it is not, however, included as a primary risk factor for violence in violence risk assessment instruments [13-17], even though some of the listed risk factors are likely to be secondary manifestations of Mental Retardation, i.e., a lack of coping skills.

1.9 SUICIDAL BEHAVIOUR AS A POTENTIAL RISK FACTOR FOR THE USE OF VIOLENCE

Higher levels of lifetime aggression have been associated with suicide attempts and completed suicide in cross-sectional and prospective studies [48]. It has been suggested that a subgroup of suicide attempters has a certain predisposition to impulsive-aggressive behaviours, a behavioural endophenotype, which may partly be explained by the shared neurobiological underpinnings [49].

1.10 NEUROLOGICAL CONDITION AS A POTENTIAL RISK FACTOR FOR THE USE OF VIOLENCE

Neurological Disorders, e.g., Epilepsy, and their significance for violent crimes have been in focus and of great interest in the history of forensic psychiatry [50], but studies have failed to demonstrate a connection with violent crimes [51]. On the other hand, traumatic brain injuries have been suggested to be a risk factor for violent crimes [52] and this is supported by a morphological imaging study identifying brain pathology in violent prisoners [53].

1.11 EARLY RISK FACTORS FOR THE USE OF VIOLENCE

Early risk factors for the use of violence include early behavioural problems variables and difficulties in upbringing conditions, often overlapping with the risk emerging from the psychiatric conditions. Episodes of violence in adulthood are often preceded by behaviour problems at a young age [54]. Youths with an early onset of such problems are typically diagnosed with Conduct Disorder, which, independently [55] or in combination with severe mental illness [56], has been shown to present an increase in the risk for violence in adulthood [57]. In addition, it has been suggested that there is a connection between childhood maltreatment and adult violence according to the ‘cycle of violence' hypothesis [58]. Negative life events and low levels of social support might also explain an increased risk of violent offending among people with common mental disorders [59]. The literature is, however, inconsistent and other studies have not found a link between childhood maltreatment and violent crime [60].

1.12 NEUROBIOLOGICAL RISK FACTORS FOR THE USE OF VIOLENCE

According to a model developed by Siever in 2008 [9], impulsive aggression may be caused by a lower threshold for the activation of motoric aggressive responses to external stimuli, without adequate reflection of the negative consequences of the behaviour. The reason for the lower threshold for aggressiveness is an imbalance between the 'top-down' control or 'brakes' provided by the orbital frontal cortex and anterior cingulate cortex, which are involved in modulating or suppressing aggressive behaviour, and excessive 'bottom-up drives' triggered by limbic regions, such as the amygdala and insula. The serotonin metabolism, shown in Figure 2, is crucial for the regulation of aggressiveness.

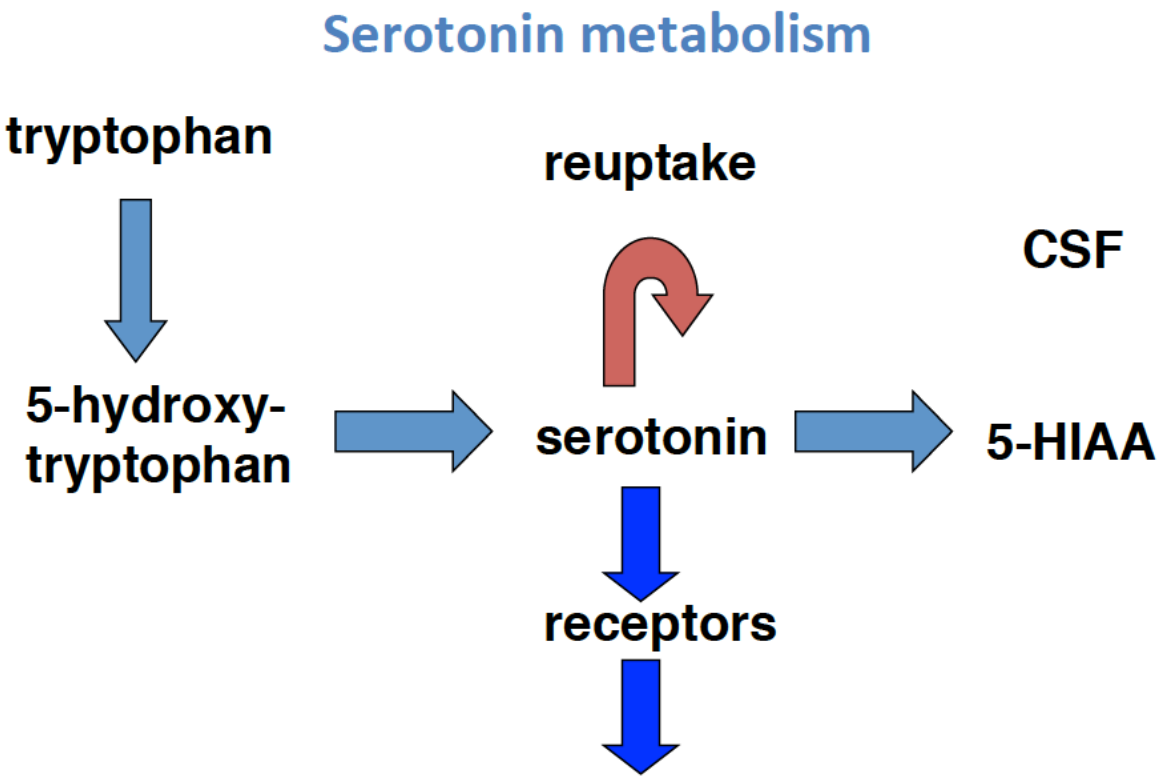

Figure 2. Serotonin metabolism.

Serotonin or 5-hydroxytryptamine (5-HT) is a monoamine neurotransmitter, biochemically derived from tryptophan. Serotonin acts on serotonin receptors in the orbital frontal cortex and anterior cingulate cortex, thereby suppressing the emergence of aggressive behaviours [9]. Serotonin thus works as an inhibitor or 'brake oil' for the aggressive impulses in the central nervous system, thereby diminishing violent behaviour. 5-hydroxyindoleacetic acid (5-HIAA) is the major metabolite of serotonin and can be detected in the cerebrospinal fluid (CSF), thus it is a proxy for the serotonin metabolism in the central nervous system. Serotonin is metabolized to 5-HIAA by the neurotransmitter-metabolizing enzyme monoamine oxidase A (MAOA).

An early study found a significant negative correlation between the concentration of CSF 5-HIAA and life-time aggressive behaviour [61] and a low CSF 5-HIAA concentration was

also associated with self-directed aggressiveness, resulting in suicide [62]. It has been suggested that a low CSF 5-HIAA concentration may be a marker of the underlying impulsivity rather than violence [63]. Non-human primate studies suggest that early environmental influences, resulting in stress, may have an enduring effect on central serotonin function with persistently lower CSF 5-HIAA concentrations and more impulsive–aggressive behaviour [64, 65]. A study of humans has reported significantly lower CSF 5-HIAA concentrations in cocaine abusing male patients with high scores on emotional neglect, indicating that childhood trauma may have an effect on central monoamine function as an adult [66].

1.13 MORTALITY AMONG THE USERS OF VIOLENCE

On examining the mortality of released prisoners, it has been shown that there is an excess mortality in different death categories among released prisoners, compared to the general population [67]. This applies particularly to persons convicted of violent crimes. In a Finnish study, habitually violent male offenders, who were considered to be dangerous to the lives of other people, the relative risk of dying was 4.9-fold compared with the normal male population during a 24.5-year period [68]. More than 10 million people are incarcerated worldwide and mental disorders are more common in prisoners than in the general population, with reports of an increased mortality from all causes after release in many countries [69]. In one study, it was shown that incarceration *per se* was not a significant predictor for premature death, meaning that the high mortality risk in sentenced offenders is independent of previous imprisonment [70].

2 AIMS

2.1 OVERALL AIMS

The overall objective of this thesis was to study the risk of interpersonal violence and violent crime in mental disorders with a focus on the effect of early risk factors and the relationship between interpersonal violence and the serotonin system, as well as the risk of death.

The specific research aims in this thesis were as follows:

2.2 STUDY I

To investigate the impact of psychiatric diagnoses and neurological disorders in late adolescence among men on convictions for violent crime later in life, taking into account early risk factors.

2.3 STUDY II

To analyse the association between childhood trauma, violent behaviour as a child and psychiatric diagnoses in relation to self-reported interpersonal violence as an adult in suicide attempters.

2.4 STUDY III

To assess the relationship between the serotonin metabolite 5-hydroxyindoleacetic acid (5-HIAA) in cerebrospinal fluid (CSF) and the exposure to violence as a child and the expressed violent behaviour in childhood and during adult life in suicide attempters.

2.5 STUDY IV

To investigate whether convictions for violent crime in men is associated with increased mortality, whether this risk is higher among those with repeated violent convictions and what the causes of death are.

3 METHODS

3.1 STUDY SETTINGS

Studies I and IV: Men conscripted for compulsory military service in Sweden during a two-day event and then followed in national registers for 35 years.

Studies II and III: Patients undergoing their clinical follow-up after a suicide attempt at the Suicide Prevention Clinic at the Karolinska University Hospital and who participated in two studies on biological and psychological risk factors for suicidal behaviour. Prior to follow-up, all the patients had been admitted to one of the psychiatric wards at the Karolinska University Hospital.

3.2 PARTICIPANTS IN THE CONSCRIPTION COHORT (STUDIES I AND IV)

The study populations consisted of 49,398 Swedish men in ***Study I*** and 48,834 Swedish men in ***Study IV,*** derived from the same conscription cohort. The men born during 1949–1951 were assessed from 1 July 1969 to 30 June 1970, i.e., at an age of 18 to 20 years, in connection with the nationwide conscription for compulsory military service. The cohort consisted of 97%–98% of all possible conscripts in Sweden at that time. The remaining young men were exempted from conscription for such medical reasons as severe physical or psychiatric disorder/disability. The follow-up time for the individuals in the cohort in official registers was 35.24 years, standard deviation (SD) = 3.98.

The conscription procedure was a two-day event, including physical tests and thorough examination by a physician to establish a physical diagnosis. Cognitive tests were performed and a psychologist interviewed all conscripts. Any suspected psychiatric disorder resulted in referral to a psychiatrist for a clinical examination and mental disorders were recorded in accordance with the International Classification of Disease, Revision 8 (ICD-8)[1]. Only main diagnoses were included in the study. Main diagnoses were defined as the most clinically relevant diagnoses determined at conscription according to ICD 8. Details of this procedure and the validity of the assessments have been described in earlier studies [71, 72]. The psychiatric conditions in the cohort were recorded in five different diagnostic groups according to the ICD-8 classification. Psychoses included diagnoses 292 and 295–298, Anxiety-Depression/neuroses 300, Personality Disorders 301, Substance-Related Disorders 303 and 304, and Mental Retardation 310–315. A sixth group with Neurological Disorders was created by grouping the following diagnoses: 309, 320, 321, 323, 324, 330, 332, 343–345 and 348. The diagnostic numbers from the ICD-8 classification are presented next.

Psychoses

292 Psychosis associated with intracranial infection
295 Schizophrenia
296 Affective psychoses
297 Paranoid states
298 Other psychoses

Anxiety-Depression/neuroses

300 Neuroses

Personality Disorders

301 Personality Disorders

Substance-Related Disorders

303 Alcoholism
304 Drug dependence

Mental Retardation

310 Borderline mental retardation
311 Mild mental retardation
312 Moderate mental retardation
313 Severe mental retardation
314 Profound mental retardation
315 Unspecified mental retardation

Neurological and other central nervous system conditions

309 Mental disorders not specified as psychotic associated with physical conditions
320 Meningitis
321 Phlebitis and thrombophlebitis of intracranial venous sinuses
323 Encephalitis, myelitis and encephalomyelitis
324 Late effects of intracranial abscess or pyogenic infection
330 Hereditary neuromuscular disorders
332 Hereditary ataxia
343 Cerebral spastic infantile paralysis
344 Other cerebral paralysis
345 Epilepsy
348 Motor neurone disease

In the total cohort of 49,398 conscripts, 9.90% (n = 4892) were diagnosed with a psychiatric or neurological condition as defined earlier. The largest diagnostic group was Anxiety-Depression/neuroses with a prevalence of 4.90% (n = 2419) in the cohort (Figure 3), followed by Personality Disorders with 2.56% (n = 1267). Mental Retardation had a prevalence of 1.06% (n = 524) and was slightly higher than Substance-Related Disorders with 0.93% (n = 459) at conscription. The smallest groups were Neurological Disorders and Psychoses with 0.39% (n = 192) and 0.063% (n = 31), respectively.

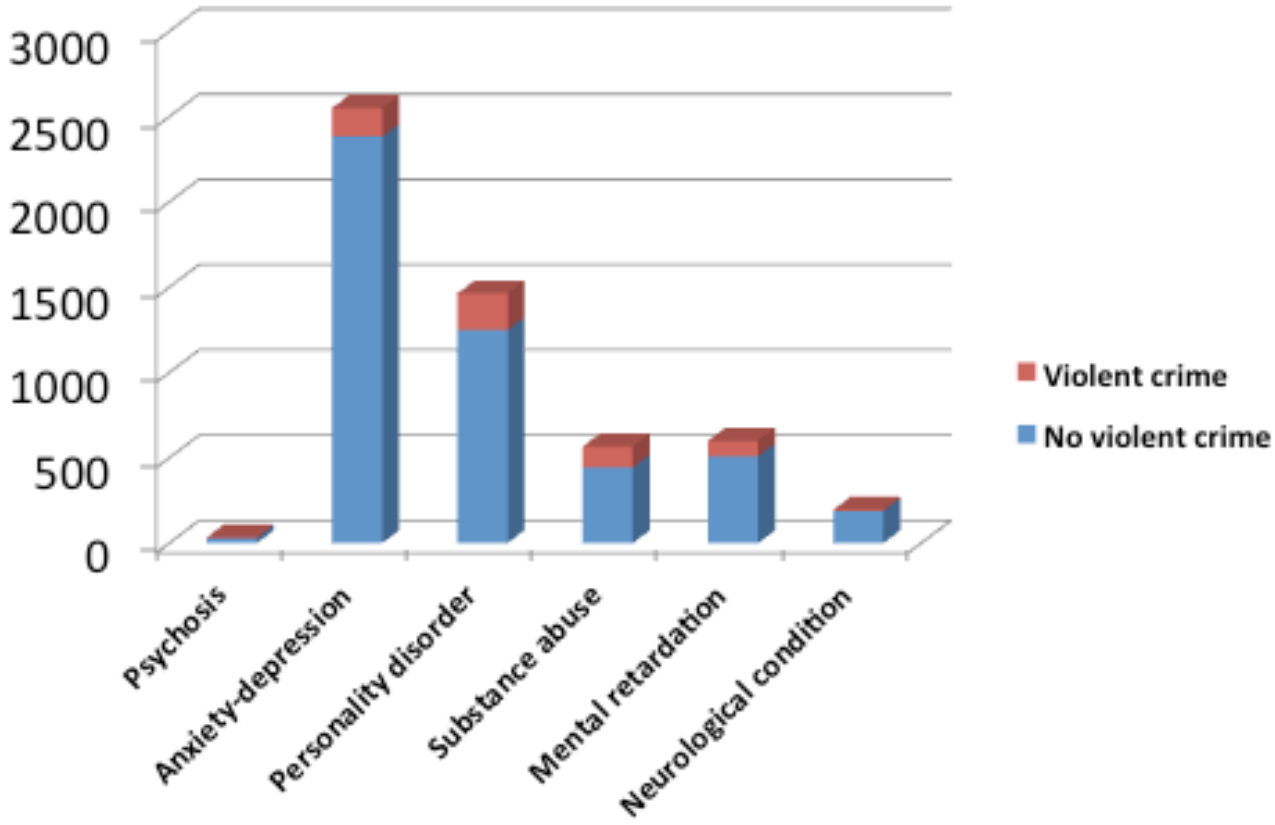

Figure 3. Diagnoses and violent crime in the conscription cohort.

3.3 PARTICIPANTS IN THE CLINICAL COHORTS (STUDIES II AND III)

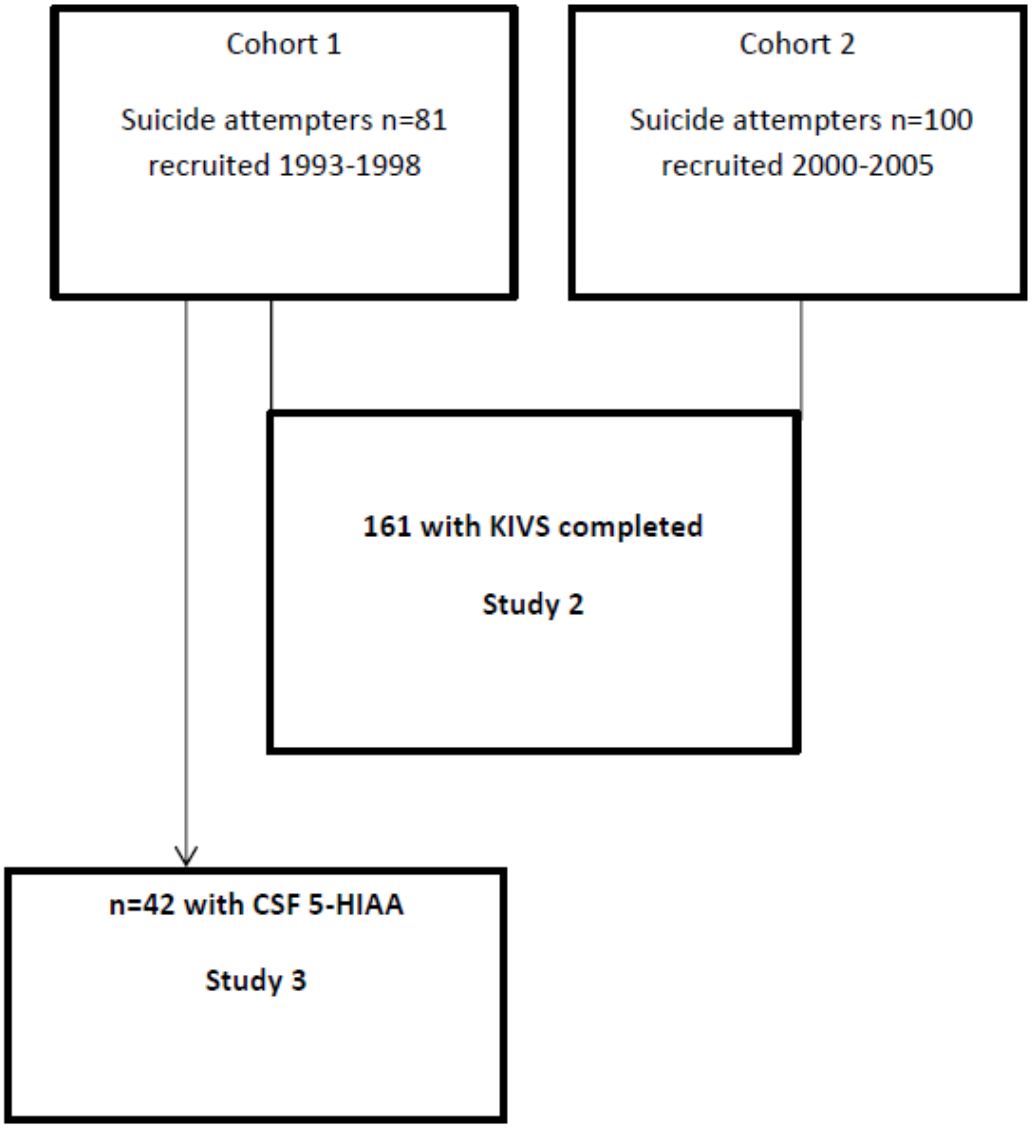

Figure 4. The clinical cohorts.

A total of 161 suicide attempters (63 men and 98 women), for whom the Karolinska Interpersonal Violence Scale (KIVS) ratings had been performed, were enrolled in ***Study II*** from two other cohorts as shown in Figure 4. Inclusion criteria were a recent suicide attempt (within one month), a fair capacity to communicate verbally and in writing in the Swedish language and an age of 18 years or older. Exclusion criteria were Schizophrenia Spectrum Psychosis, Intravenous Drug Abuse, Dementia and Mental Retardation. The cohort and the Karolinska Interpersonal Violence Scale have been described in details in another study [48]. Patients were recruited between the years 1993 and 2005 from the catchment area of the psychiatric clinic at the Karolinska University Hospital. During the first study period (1993–1998), exact information on the sampling procedure with the participation rate was not registered. During the second study period (2000–2005), 258 patients (169 women and 89

men) from the catchment area made a suicide attempt and came into contact with the Suicide Prevention Clinic. Sixty-one patients were excluded due to the exclusion criteria, 50 did not want to participate in the study and 47 were not offered to participate due to such reasons as early refusal to have a clinical follow-up, holiday period or moving to another part of the country. A total of 100 suicide attempters (67 women and 33 men) were enrolled in Study II during the second study period. The mean age of the patients was 35 years (SD = 12.1; range 18–69) and did not differ between men and women. Thirty-two patients (20%) had used a violent suicide attempt method (14 women, 14.3% and 18 men, 28.6%). A suicide attempt was defined as a self-destructive act with some degree of intent to die, and the suicide attempt method was defined as violent or not according to the criteria of Träskman et al. [73].

Ninety-five healthy volunteers (38 men and 57 women) were recruited to ***Study II*** in Stockholm, 2003–2004. They were screened by a psychiatrist to verify the absence of a current mental disorder. The mean age of the healthy volunteers was 40 years (SD = 11, range 18–63).

To establish the diagnoses according to the Diagnostic and Statistical Manual of Mental Disorders, third revised (DSM-III-R) and fourth (DSM-IV) editions, the participants were interviewed by a trained psychiatrist using the research version of the Structured Clinical Interview for DSM-III-R or DSM-IV, Axis I (SCID I) [2, 3]. Trained clinical psychologists established Axis II, i.e., Personality Disorder diagnoses with an SCID II interview [4, 5]. Ninety-five per cent of the suicide attempters had at least one current Axis I or II psychiatric diagnosis. Of the patients, 78% fulfilled the criteria for Mood Disorders (Major Depressive Disorder, Single Episode or Recurrent, Bipolar Disorder, Depressed or Dysthymic Disorder), 5% for Adjustment Disorder and 5% for Anxiety Disorders (half of them with Post Traumatic Stress Disorder). Three per cent of the patients had a Substance-Related Disorder as their major diagnosis, but 25% of the patients had a co-morbid lifetime diagnosis of Substance-Related Disorder (83% Alcohol Dependence). SCID II interviews were not performed in six patients. Among Axis II diagnoses, 55 patients (36%) fulfilled criteria for a Personality Disorder, 42% of them in Cluster B. Most patients with a Personality Disorder had a diagnosis of Borderline Personality Disorder (n = 19) or Personality Disorder Not Otherwise Specified (n = 20). Eleven patients fulfilled the criteria for a Conduct Disorder during childhood and seven patients for Antisocial Personality Disorder. Table 1 shows the diagnostic grouping of suicide attempters in Study II with regard to the degree of co-morbidity.

Table 1. Diagnostic grouping of suicide attempters in Study II.

DSM diagnostic groups	**Number of suicide attempters**
No DSM diagnosis	8
DSM Mood- or Anxiety Axis I diagnosis without co-morbid Substance Abuse or Personality Disorder	74
DSM Mood- or Anxiety Axis I diagnosis with co-morbid Substance Abuse only	18*
DSM Mood- or Anxiety Axis I diagnosis with co-morbid Personality Disorder only	35*
DSM Mood- or Anxiety Axis I diagnosis with both co-morbid Substance Abuse and Personality Disorder	20*

*Four patients not fulfilling the criteria for Mood or Anxiety diagnosis, but only criteria for Substance Abuse and/or Personality Disorder were included in the groups 3, 4 and 5, respectively.

Six patients were not diagnosed for Axis II and were not included in the analysis. Diagnostic groups did not overlap.

Study III involved 42 medication-free suicide attempters (15 men, mean age 45 years, S.D . =12.8, range 22–69 and 27 women, mean age 36 years, S.D. = 12.6, range 18–68; $p < 0.1$). Inclusion and exclusion criteria were the same as in Study II, as well as the diagnostic procedure, but only DSM-III-R was used for classification [3, 5] and not DSM-IV. Ninety-five per cent of participants had at least one current Axis I psychiatric diagnosis; 78% of the patients fulfilled criteria for Mood Disorders (Major Depressive Disorder, Single Episode or Recurrent, Bipolar Disorder, Most Recent Episode Depressed or Dysthymic Disorder), 7% for Adjustment Disorder and 5% for Anxiety Disorders, one patient had a Substance-Related Disorder and one an Unspecified Psychiatric Disorder (Not Psychotic). Nineteen per cent of the patients had a co-morbid Substance-Related Disorder (mostly Alcohol Dependence). Among Axis II diagnoses, 37% of the patients met the criteria for a Personality Disorder (38% Cluster B).

3.4 MEASUREMENTS AT CONSCRIPTION OF OTHER POTENTIAL RISK FACTORS THAN DIAGNOSIS FOR THE VIOLENT CRIMES (STUDY I)

Based on the literature on violence risk assessment, additional risk factors (confounders) were selected from the conscription data using the following procedure. Five risk assessment instruments, i.e., the Level of Service Inventory – Revised (LSI-R) [13], the Psychopathy Checklist – Revised (PCL-R) [14], the Historical-Clinical-Risk Management-20, Version 3 (HCR-20^{V3}) [15], the Spousal Assault Risk Assessment: Short Version (SARA: SV) [16] and the Violence Risk Screening-10 (V-RISK-10) [17], were scrutinized and 124 variables were clustered into 21 domains. Each participant completed two non-anonymous self-report questionnaires with a total of 105 questions. The questionnaires have been found to have sufficient validity for epidemiological studies [74-77]. The questions and the data obtained from these questionnaires were assessed. The answers from 31 of these items were statistically significantly associated with risk of future convictions for violent crime. Therefore, these 31 items, containing information corresponding to 30 variables in eleven domains of the violence risk assessment instruments, were chosen as potential additional risk factors/confounders. The question/variable from each domain that was most significantly associated with a conviction for violent crime was selected; only three questions were not included in the study because of there only being a weak association. The following eight items from the conscription questionnaires were used for further analyses: Poor economic conditions in the family, Divorced parents, Corporal punishment in upbringing, Easily angry, Sleep disturbance (i.e., reflecting stress), Lowered marks due to misconduct at school, Contact with the police or child welfare section of a municipal welfare committee (referral to the child welfare section was due to either the child's misconduct problems or maltreatment in the family) and Arrested by police for drunkenness (Figure 5). The last of these risk factors was not excluded despite the fact that Substance-Related Disorders were among the analysed diagnoses because the variable itself was considered to reflect a certain type of behaviour not always caught in a Dependence diagnosis. The following domains of risk factors derived from the literature on risk assessment instruments did not have corresponding information in the conscription data: Criminal history as an adult, Bad conduct in prison or under probation, Unemployment, Economic problems as an adult, Marital problems or promiscuous sexual behaviour, Living in an area with high criminality, Having friends with a criminal history, Negative attitudes toward legal systems, or a rating for Psychopathy or lack of empathy.

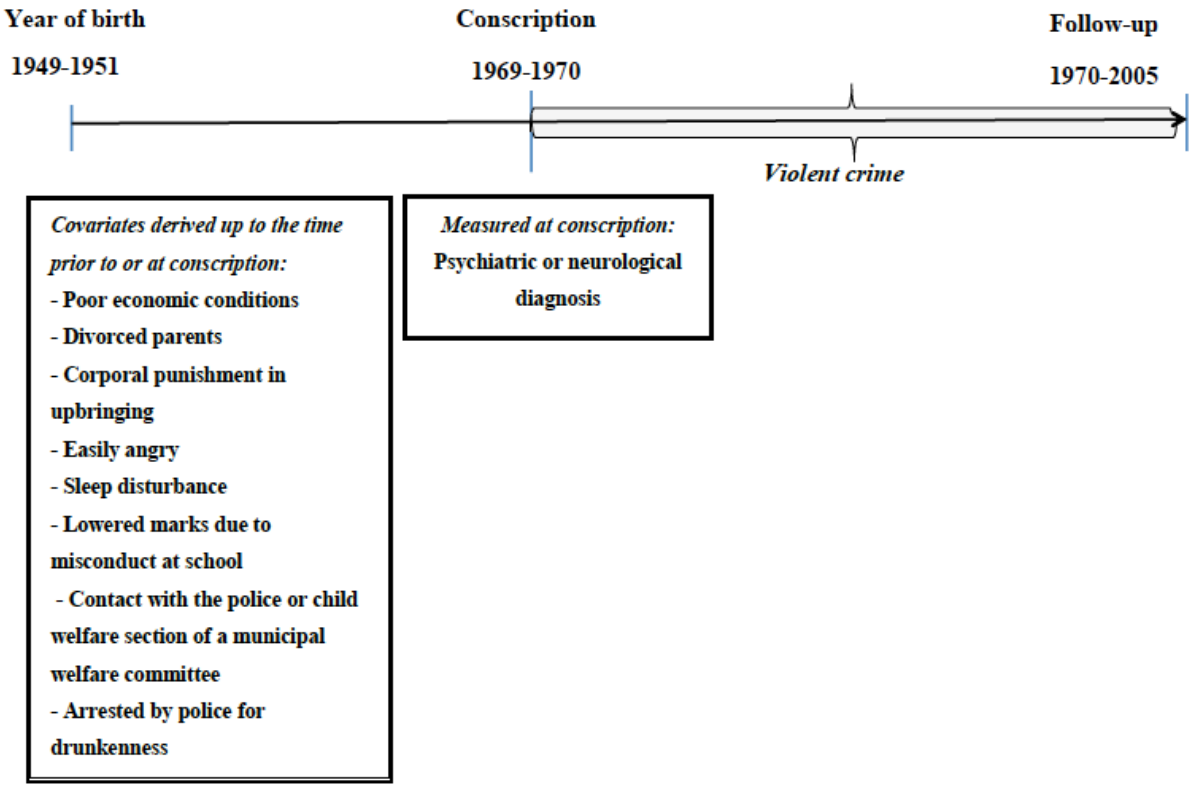

Figure 5. An illustration of possible predictors of violent crime in Study I.

3.5 MEASUREMENTS OF POTENTIAL RISK FACTORS FOR MORTALITY AT CONSCRIPTION (STUDY IV)

Based on earlier studies of risk factors for violence and mortality, we first included 19 variables associated with both lifetime violent offending and mortality as potential confounders for multivariate analyses. After a bivariate Cox proportional regression analysis, we selected, as depicted in Figure 6, ten significant variables from the psychiatric and psychological evaluations and from the questionnaires as confounders for the multivariate analyses. The psychiatric diagnosis at conscription, defined as Yes (one or more diagnoses) vs No, was chosen. Each participant was seen by a military psychologist for an interview and assessed on a series of variables. The measures were assessed on a 1–5-point Likert scale (5 being the highest), yielding a distribution corresponding to 7%, 24%, 38%, 24% and 7% for scale points 1, 2, 3, 4, and 5, respectively. The ratings by the psychologists were regularly checked for inter-rater reliability in order to check for good quality [77]. The included psychological variables were Emotional control (a summary of assessed mental stability, emotional capacity and tolerance to stress and frustration) and Social maturity (feeling responsibility for activities by other persons, and having a sense of independence and a degree of social extroversion). The two variables were assessed on the five-point scale, with 1 = very bad; 2 = bad; 3 = moderate; 4 = good; 5 = very good, with the categorizations Emotional control 1–2 vs 3–5 and Social maturity 1–2 vs 3–5. The following items from the

conscription questionnaires were used for further analyses: Divorced parents (Yes vs No), Contact with the police or child welfare section of a municipal welfare committee (Yes vs No), Lowered marks due to misconduct at school (Yes vs No), Ever run away from home (Yes vs No) and Smoking (≥ 10 cigarettes/day vs < 10 cigarettes/day or none). Also included were Problem drinking (Yes vs No, with ' Yes' defined as consumption of ≥ 210 g pure alcohol per week, being intoxicated often, and/or having been apprehended for public drunkenness on at least one occasion) and Drug misuse, defined as having used illicit drugs 10 times or more or having used drugs intravenously one or more times vs less than ten times or no use.

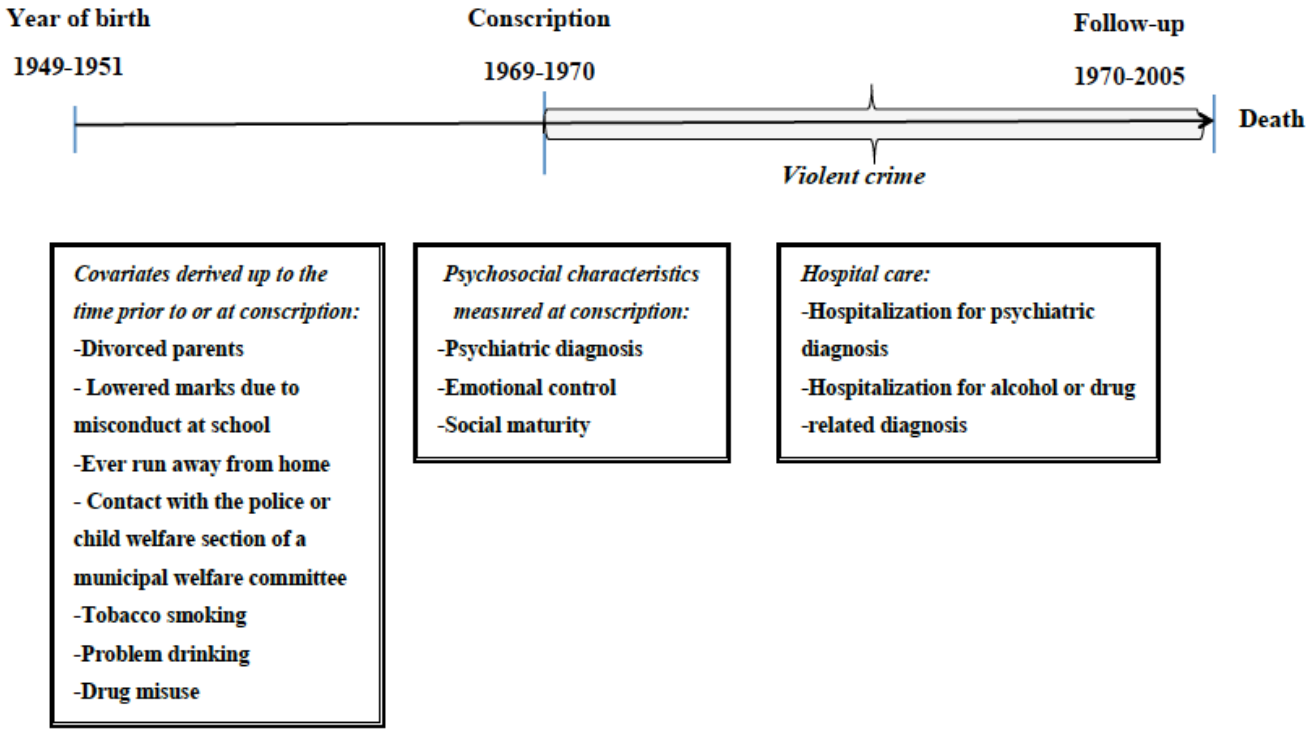

Figure 6. An illustration of possible predictors of mortality in Study IV.

3.6 MEASUREMENT OF INPATIENT CARE AFTER CONSCRIPTION (STUDY IV)

Data from the National Inpatient (Hospital) Register were used to identify inpatient care according to ICD-8 [1] and ICD-9 [6] from 1987 and ICD-10 [7] from 1997 onwards. The National Inpatient (Hospital) Register includes details of inpatient care and covers all public hospitals in Stockholm and Uppsala County since 1972, 85% of all Swedish public inpatient care stays since 1983 and more than 99% of such care stays since 1987. The diagnoses of interest for identifying inpatient care in this study were (ICD classifications in brackets): Alcohol-Related diagnoses (ICD-8: 291, 303, 571.00, 571.01 and 980; ICD-9: 291, 303, 305A, 357F, 425F, 535D, 571A-571D and 980; and ICD-10: E24.4, F10, G31.2, G62.1, G72.1, I42.6, K29.2, K70, K86.0, O35.4, P04.3, Q86.0, T51, X45, Y91, Z50.2 and Z71.4),

Drug-Related diagnoses (ICD-8: 304 and 965.0; ICD-9: 304, 965A, 968F, 969G and 969H; and ICD-10: F11-12, F14, F15, F16, F18, F19, O35.5, P04.4, T40.0 T40.3, T40.5-T40.9, T43.6, Z71.5, and X42) and Psychiatric disorders (ICD-8, and ICD-9 290-319 and ICD-10: F00-F69).

3.7 MEASUREMENT OF VIOLENT CRIMES AFTER CONSCRIPTION (STUDIES I AND IV)

Using the conscripts' unique Swedish civic registration numbers, the cohort was linked by record to the National Crime Register, which contains information on convictions in Sweden from 1966 onwards. Data were obtained to identify the date, type and number of criminal offences during the years 1971–2006. The register covers more than 99% of all crimes in Sweden. The studied outcome measure was a conviction for a violent crime based on the Swedish Penal Code categorisation of violent crime (n = 2532), which was defined as homicide (n = 22), manslaughter (n = 135), aggravated assault (n =162), assault and battery (n = 2102), bodily harm (n = 107) and other (n = 4). Sex crimes and robbery were not included in the category of violent convictions. Violent convictions were categorized as follows: conviction for violence (at least one vs none), where no violent crime was defined as all other convictions or a lack of any conviction. We also categorized offences according to the number of convictions for violent crime (one vs two or more) in ***Study I*** and violent recidivism (two or more convictions vs none) in ***Study IV***.

3.8 MEASUREMENT OF MORTALITY (STUDY IV)

Mortality data came from the Cause of Death Register, which covers more than 99% of all deaths occurring in Sweden and is based on information from death certificates. Underlying causes of death are classified according to ICD-8, ICD-9 and ICD-10, as for the National Inpatient (Hospital) Register. One underlying cause of death is given on each death certificate, although contributing causes can be added. The ICD numbers for Alcohol-Related diagnoses, Drug-Related diagnoses and Psychiatric disorders for cause of death were the same as for inpatient care in Paragraph 3.6.

3.9 MEASUREMENTS OF THE EXPOSURE TO VIOLENCE AND THE USE OF VIOLENCE (STUDIES II AND III)

The Karolinska Interpersonal Violence Scale (KIVS), presented in Figure 7, contains four subscales assessing both exposure to violence and expressed violent behaviour in childhood (6–14 years of age) and during adult life (15 years or older). The ratings are based on a semi-structured interview. Interviews and ratings (0–5 for each subscale, total 20) were performed and assessed by trained clinicians. The Buss–Durkee Hostility Inventory, the 'Urge to act out hostility' subscale from the Hostility and Direction of Hostility Questionnaire (HDHQ) and the Early Experience Questionnaire (EEQ) have been used for validation of KIVS and the inter-rater reliability for the KIVS subscales was high [48]. Ratings on the subscale 'Used interpersonal violence as an adult' were dichotomized in ***Study II***: non-violent patients (0, 1, 2) and violent patients (3, 4, 5).

The Karolinska Interpersonal Violence Scale[a]

The steps of this scale are defined by short statements about violent behavior. On the basis of an interview with the subject, use the highest score where one or more of the statements apply.

A. Used violence.

As a child (6–14 years)

0 No violence.
1 Occasional fights, but no cause for alarm among grown-ups in school or in the family.
2 Fighter. Been in fights a lot.
3 Often started fights. Hit a comrade who had been bullied. Continued hitting when the other had surrendered.
4 Initiated bullying. Often hit other children, with fist or object.
5 Caused serious physical injury. Violent toward adult(s). Violent behavior that led to intervention by social welfare authorities.

As an adult (15 years or older)

0 No violence.
1 Slapped or spanked children on occasion. Shoved or shook partner or another adult.
2 Occasionally smacked partner or child. Fought when drunk.
3 Assaulted partner drunk or sober. Repeated corporal punishment of child. Frequent fighting when drunk. Hit someone when sober.
4 Instance of violent sexual abuse. Repeated battering/physical abuse of child or partner. Assaulted/attacked other persons frequently, drunk or sober.
5 Killed or caused severe bodily harm. Repeated instances of violent sexual abuse. Convicted of crime of violence.

B. Victim of violence.

Childhood (6–14 years)

0 No violence.
1 Occasional slaps. Fights in school, of no great significance.
2 Bullied occasionally for short period(s). Occasionally exposed to corporal punishment.
3 Often bullied. Frequently exposed to corporal punishment. Beaten by drunken parent.
4 Bullied throughout childhood. Battered/beaten up by schoolmates. Regularly beaten by parent or another adult. Beaten with objects. Sexually abused.
5 Repeated exposure to violence at home or in school that resulted at least once in serious bodily harm. Repeated sexual abuse, or sexual abuse that resulted in bodily harm.

Adulthood (15 years or older)

0 No violence.
1 Threatened or subjected to a low level of violence on at least one occasion.
2 Beaten by partner on occasion. Victim of purse snatching. Threatened with object.
3 Threatened with a weapon. Robbed. Beaten by someone other than partner. Frequently beaten by partner.
4 Raped. Battered.
5 Repeatedly raped. Repeatedly battered. Severely battered, resulting in serious bodily harm.

[a]© Copyright 2010, Jussi Jokinen, MD, PhD. The Swedish version of the Karolinska Interpersonal Violence Scale (KIVS) was translated into English by an authorized bilingual translator; the English version of the KIVS was then back-translated into Swedish and the equivalence was checked by the original authors. Copies can be obtained from the author.

Figure 7. The Karolinska Interpersonal Violence Scale (KIVS).

3.10 MEASUREMENT OF THE SEVERITY OF DEPRESSION (STUDY III)

To evaluate the severity of Depression, the Montgomery–Åsberg Depression Rating Scale (MADRS) was used [78].

3.11 MEASUREMENT OF THE SEROTONIN METABOLITE 5-HYDROXYINDOLEACETIC ACID IN CEREBROSPINAL FLUID (STUDY III)

Lumbar punctures were performed in a standardized manner between 8 and 9 a.m. after fasting in bed since midnight. Twelve millilitres of cerebrospinal fluid (CSF) were withdrawn with the patient in the sitting position, the needle being inserted between lumbar vertebrae IV and V. The CSF was immediately centrifuged and stored at -80^0C. CSF 5-HIAA was analysed using mass fragmentography (GC-MS) according to methods developed by Bertilsson [79]. The coefficient of variation of the analytical method is less than 5%.

3.12 STATISTICAL ANALYSES

Study I: The relative risks of convictions for violent crime during the years 1970–2006 were examined in relation to psychiatric and neurological diagnoses and other risk factors at conscription from 1 July 1969 to 30 June 1970, as measured by odds ratios (ORs) with 95% confidence intervals (CIs) from bivariate and multivariate logistic regression analyses. The outcome measure was any conviction for violent crime. In the bivariate analyses, the reference categories comprised all individuals without any psychiatric or neurological diagnosis or without any other risk factor at conscription, with the independent variables being measured only once. Only significant diagnostic and other risk factor variables in the bivariate analyses were included in the multivariate analyses. Potential confounders/other risk factors for the bivariate and multivariate analyses were selected by testing for all other possible risk factors using chi-square tests (categorical variables) and retaining the one in each domain that was the most significant predictor of conviction for a violent crime. Tests for non-parametric correlations using Spearman's rho verified that the risk factors (i.e., ordinal variables from questionnaires) did not correlate with each other. Group differences concerning age of onset of violent disorder convictions were tested with the Kruskal-Wallis test. The p-value was set at < 0.05 in all the analyses. We used SAS version 9.1 (SAS Institute Inc., Cary, NC, USA) for all the statistical analyses in Study I.

Study IV: Cox proportional bivariate and multivariate regression analyses were used to calculate the hazard ratios (HRs) in violent offenders and all other conscripts for mortality and causes of death from 1 January 1970 up to the time of death or to the end of the observation period (31 December 2004). The person times were calculated for all persons as mentioned above, including those with violent crime episodes during the time period. In order to analyse the impact of violence offence on mortality and causes of death, we performed multivariate Cox regression analyses, adjusted for early risk factors including alcohol and drug misuse in relation to the outcomes. The early covariates were measured at the time of conscription and the exposure variable (violence) occurred from 1970 onwards (see Figure 6). In the multivariate models, we included only those variables which were significant in the

bivariate analyses. We used SAS, version 9.2 (SAS Institute Inc., Cary, NC, USA) for all the statistical analyses in Study IV.

Study II: Initial analyses were carried out to evaluate skewness and kurtosis of the distributions with the Shapiro-Wilk test. Tests of non-parametric correlations were performed using Spearman rho. Non-parametric statistics, including the Kruskal-Wallis or Wilcoxon test, were applied for between-group comparisons. Based on the results of univariate analyses, standard multivariate logistic regression analyses were conducted using the two KIVS ratings, Exposure to violence as a child and Expressed violence as a child, together with Substance Abuse diagnosis, Personality Disorder diagnosis and Age as possible predictors of adult interpersonal violence. To be defined as violent as an adult, a violence score of 3 or above on the KIVS subscale Expressed violence as an adult was applied. Since many studies of violent and suicidal behaviour have shown gender differences and there were gender differences on the KIVS subscale Expressed violence as a child, we stratified for men and women separately. An *ad hoc* Receiver Operating Characteristics (ROC) analysis was used to find optimal thresholds for significant clinical predictors of adult violence. ROC curves and tables were created to establish the optimal cut-off values. ROC areas under the curves (AUCs) were calculated as a measure of the diagnostic performance. The cut-off point that optimized sensitivity (proportion of violent patients correctly identified) and specificity (proportion of non-violent patients correctly identified) was applied. Pearson's chi-square and Fisher's exact test were used for cross-tabulations of categorical variables. The p-value was set at < 0.05. We used the Statistical Package JMP 9 software (SAS Institute Inc., Cary, NC, USA) for all the statistical analyses in Study II.

Study III: The Shapiro-Wilk test was used to test whether data were normally distributed. For comparisons between two groups (dichotomized groups of suicide attempters with CSF 5-HIAA above or under the median), Student's t-test was used for parametric data and the Kruskal-Wallis test for non-parametric data. For multiple parametric comparisons, a one-way analysis of variance (ANOVA) was used; tests of parametric correlations were performed using Pearson's r and non-parametric correlations using Spearman's rho. Fisher's z-test was used to compare correlation coefficients (Pearson's r). The p-value was set at < 0.05 in all the analyses. We used the Statistical Package JMP 9 software (SAS Institute Inc., Cary, NC, USA) for all the statistical analyses in Study III.

3.13 ETHICAL CONSIDERATIONS

Studies I and IV: The Regional Ethical Review Board in Stockholm approved the study protocols (Dnr 2007/174-31, Dnr 2008/1086-31/5). The cohort was followed via official registers and conviction data were linked at Statistics Sweden via the unique Swedish civic registration number for each individual in the cohort. This number was then replaced with an individual serial number, making the data anonymous to the researchers. Use of this procedure to guarantee the anonymity of data made it unnecessary for the participants to sign their informed consent. The Ethics Committee was aware of the fact that we were not going to obtain consent from the participants when they approved the study.

Studies II and III: The Regional Ethical Review Board in Stockholm approved the study protocols (Dnr 93-211 and Dnr 00-194) and the participants signed informed consent forms. Suicide attempters are a clinical high-risk group concerning suicide risk. When proposing participation in the study, it was emphasized that participation did not have any effect on the participants' clinical follow-up at the Suicide Prevention Clinic.

The risk of infringement of privacy was extremely small because the data management and analyses were performed under confidential forms and only authorized personnel assessed the collected data.

The current research can help to better identify risk factors for violent behaviour which may stigmatize psychiatric patients. Identifying risk factors for interpersonal violence among psychiatric patients may, however, help to facilitate better care for aggressive individuals and thereby reduce the suffering for themselves and the surrounding individuals who are subjected to the violence. The current research has also focused on the relationship between violent crime and the mortality among offenders and to emphasize violent criminals' suffering and death may be de-stigmatizing. Moreover, through the present studies, we were able to gain more knowledge about the risk factors for the mortality of violent offenders, which could improve the care and thereby the survival of the group of violent criminals.

4 RESULTS

4.1 STUDY I

4.1.1 Psychiatric diagnoses and future convictions for violent crime

Fifteen per cent of the men with a psychiatric diagnosis at conscription had been convicted of at least one violent crime during the follow-up period, compared to 3.7% of the conscripts without a psychiatric diagnosis. There was a significant association between receiving a psychiatric diagnosis at conscription and a future conviction for violent crime (odds ratio [OR] 3.83, 95% confidence interval [CI] 3.47–4.22). The analyses of specific psychiatric diagnostic groups revealed that Substance-Related Disorders had the strongest association with convictions for violent crime (OR 10.08, 95% CI 8.18–12.42), followed by Mental Retardation (OR 5.65, 95% CI 4.50–7.09) and Personality Disorders (OR 5.36, 95% CI 4.60–6.25). Anxiety-Depression (OR 1.99, 95 % CI 1.69–2.34) and Psychosis (3.83, 95% CI 1.34–10.96) had a weaker association with violent crime convictions.

4.1.2 Neurological conditions and future convictions for violent crime

Among persons with Neurological diagnoses, 3.7% were convicted for violent crimes during the follow-up. There was no significant association between Neurological conditions and future convictions for violent crime (OR 1.03, 95% CI 0.48–2.21).

4.1.3 Other risk factors relevant to future convictions for violent crime

Table 2 shows bivariate logistic regression analyses between other selected potential risk factors, measured at conscription, and future convictions for violent crime. Arrested by police for drunkenness had the strongest association with future convictions for violent crime (OR 5.91, 95% CI 5.36–6.50), followed by Contact with the police or a child welfare committee (OR 5.32, 95% CI 4.87–5.82).

Table 2. Bivariate logistic regression analyses for future convictions for violent crime.

Variables	**Violent crime** **OR (95% CI)**
Poor economic conditions in family (very or rather poor vs average, rather or very good)	1.42 (1.24–1.64)
Divorced parents (Yes vs No)	2.87 (2.60–3.18)
Corporal punishment in upbringing (often or sometimes vs seldom or never)	1.96 (1.76 – 2.18)
Easily angry (often vs sometimes, seldom or never)	3.13 (2.80–3.51)
Sleep disturbance (often vs sometimes, seldom or never)	1.76 (1.52–2.04)
Lowered marks due to misconduct at school (several times or once vs never)	3.92 (3.61–4.27)
Contact with the police or child welfare committee (several times or sometimes vs never)	5.32 (4.87–5.82)
Arrested by police for drunkenness (several times, twice or once vs never)	5.91 (5.36–6.50)

4.1.4 Multivariate regression analyses

Table 3 shows the multivariate logistic regression analyses in Models I–IV. Individuals meeting the diagnostic criteria for Psychosis were relatively few (n = 31). When this diagnostic group was included in the different models and adjusted for potential confounders in the multivariate analyses in the preliminary analyses, there was no significant association with violent convictions in any of the models and the confidence intervals were spread. Consequently, it was decided that the number of persons meeting the diagnostic criteria for Psychosis was too small and therefore the group was not included in the final multivariate analyses. The remaining four groups of psychiatric diagnoses were included (Model I) with successive addition of and stepwise adjustment with other potential risk factors in upbringing conditions (Model II), personal factors (Model III) and early behavioural problem variables (Model IV), respectively. Of all the diagnoses, Substance-Related Disorders had the strongest association with future convictions for violent crime in Models I–III, followed by Mental Retardation and Personality Disorders. In the fully adjusted model, Mental Retardation had the strongest association with future convictions for violent crime (OR 3.60, 95% CI 2.73–4.75), followed by Substance-Related Disorders (OR 2.81, 95% CI 2.18–3.62) and Personality Disorders (OR 2.66, 95% CI 2.21–3.19), while Anxiety-Depression only had a weak, but significant, association (OR 1.29, 95% CI 1.07–1.55).

On considering other risk factors than psychiatric diagnoses in the fully adjusted model, early behavioural problem variables had the strongest association with future convictions for violent crime. The variables Divorced parents, Corporal punishment in upbringing and Easily angry were also significantly associated with a future conviction for violent crime, but to a lesser extent, whereas Poor economic conditions in family and Sleep disturbance did not show any significant association with future convictions for violent crime in this study.

Table 3. Multivariate logistic regression analyses for future convictions for violent crime in Models I–IV.

	Model I OR (95%CI)	Model II OR (95%CI)	Model III OR (95%CI)	Model IV OR (95%CI)
Anxiety-Depression (Yes vs No)	1.99 (1.69–2.34)	1.79 (1.51–2.12)	1.63 (1.37–1.94)	1.29 (1.07–1.55)
Personality Disorder (Yes vs No)	5.36 (4.60–6.25)	4.90 (4.16–5.76)	4.29 (3.62–5.08)	2.66 (2.21–3.19)
Substance-Related Disorder (Yes vs No)	10.08 (8.18–12.42)	8.18 (6.53–10.26)	7.55 (5.98–9.54)	2.81 (2.18–3.62)
Mental Retardation (Yes vs No)	5.65 (4.50–7.09)	4.95 (3.87–6.33)	4.39 (3.40–5.67)	3.60 (2.73–4.75)
Poor economic conditions in family (very or rather poor vs average, rather or very good)		1.00 (0.86–1.17)	0.98 (0.84–1.15)	1.00 (0.85–1.18)
Divorced parents (Yes vs No)		2.32 (2.08–2.59)	2.30 (2.06–2.58)	1.68 (1.49–1.90)
Corporal punishment in upbringing (often or sometimes vs seldom or never)		1.61 (1.43–1.80)	1.52 (1.35–1.71)	1.29 (1.14–1.46)
Easily angry (often vs sometimes, seldom or never)			2.15 (1.89–2.45)	1.72 (1.50–1.98)
Sleep disturbance (often vs sometimes, seldom or never)			0.93 (0.78–1.11)	0.84 (0.70–1.01)
Lowered marks due to misconduct at school (several times or once vs never)				2.11 (1.91–2.34)
Contact with the police or child welfare committee (several times or sometimes vs never)				2.67 (2.38–2.99)
Arrested by police for drunkenness (several times, twice or once vs never)				2.06 (1.82–2.32)

Model 1. Model fit: Chi-square = 798.98, DF = 4, $p < 0.0001$; p-values of all included predictors < 0.0001. **Model 2.** Model fit: Chi-square = 1032.38, DF = 7, $p < 0.0001$; p-values of all included predictors except Poor economic conditions in family ($p = 1.00$) were significant, $p < 0.0001$. **Model 3.** Model fit: Chi-square = 1128.36, DF = 9, $p < 0.0001$; p-values of all included predictors except Poor economic conditions in family ($p = 0.80$) and Sleep disturbance ($p = 0.44$) were

significant, $p < 0.0001$. **Model 4.** Model fit: Chi-square = 2231.10, DF = 12, $p < 0.0001$; p-values of all included predictors except Poor economic conditions in family ($p = 0.98$) and Sleep disturbance ($p = 0.058$) were significant: Anxiety-Depression, $p = 0.0074$, all other p values < 0.0001.

4.1.5 Onset of and relapse in violent crimes

The mean (standard deviation [SD]) age of onset for a future conviction for violent crime after conscription in the group with no psychiatric diagnoses was 26.5 (8.1) years. The mean age of onset was significantly lower for subjects diagnosed with Substance-Related Disorders, Personality Disorders and Mental Retardation with 21.5 (3.6), 21.9 (4.7) and 23.4 (5.7) years, respectively, compared to the group without any psychiatric diagnoses ($p < 0.001$). The age of onset for conscripts with Anxiety-Depression diagnoses was 25.9 (8.1), which did not statistically significantly differ from individuals without any psychiatric diagnosis ($p = 0.0825$). The regression analysis was repeated in a fully adjusted multivariate model with the outcome of at least one violent crime relapse. The results of this analysis showed that individuals with Mental Retardation (OR 4.02, 95% CI 2.60–6.22), Personality Disorder (OR 3.67, 95% CI 2.81–4.79) and Substance Abuse (OR 2.99, 95% CI 2.06–4.32) had significantly higher risks of violent crime relapse compared to subjects diagnosed with Anxiety-Depression (OR 1.40, 95% CI 1.03–1.89). There was also a stronger association with recidivism in violent crime for the other relevant risk factors; this was particularly evident for early behavioural problem variables.

4.2 STUDY II

4.2.1 Psychiatric diagnoses, co-morbidity and the expressed violence as an adult

Patients reported significantly more use of adult violence than healthy controls ($p < 0.0001$, Kruskal-Wallis). Ninety-five per cent of suicide attempters fulfilled the criteria for at least one DSM diagnosis (Axis I or II). These patients reported significantly more adult interpersonal violence than suicide attempters without any DSM diagnosis ($n = 8$; $p = 0.03$, Wilcoxon test).

Figure 8 shows group comparisons between healthy controls and patients divided in diagnostic categories concerning degree of co-morbidity and use of interpersonal violence as an adult ($p < 0.0001$, Kruskal-Wallis). Suicide attempters with a Mood or Anxiety diagnosis, with both co-morbid Substance Abuse and Personality Disorder reported the highest levels of adult interpersonal violence, and they had significantly higher scores for use of adult violence than suicide attempters with only Mood or Anxiety Disorder ($p = 0.0025$ Wilcoxon test) and suicide attempters with co-morbid Personality Disorder ($p = 0.047$, Wilcoxon test).

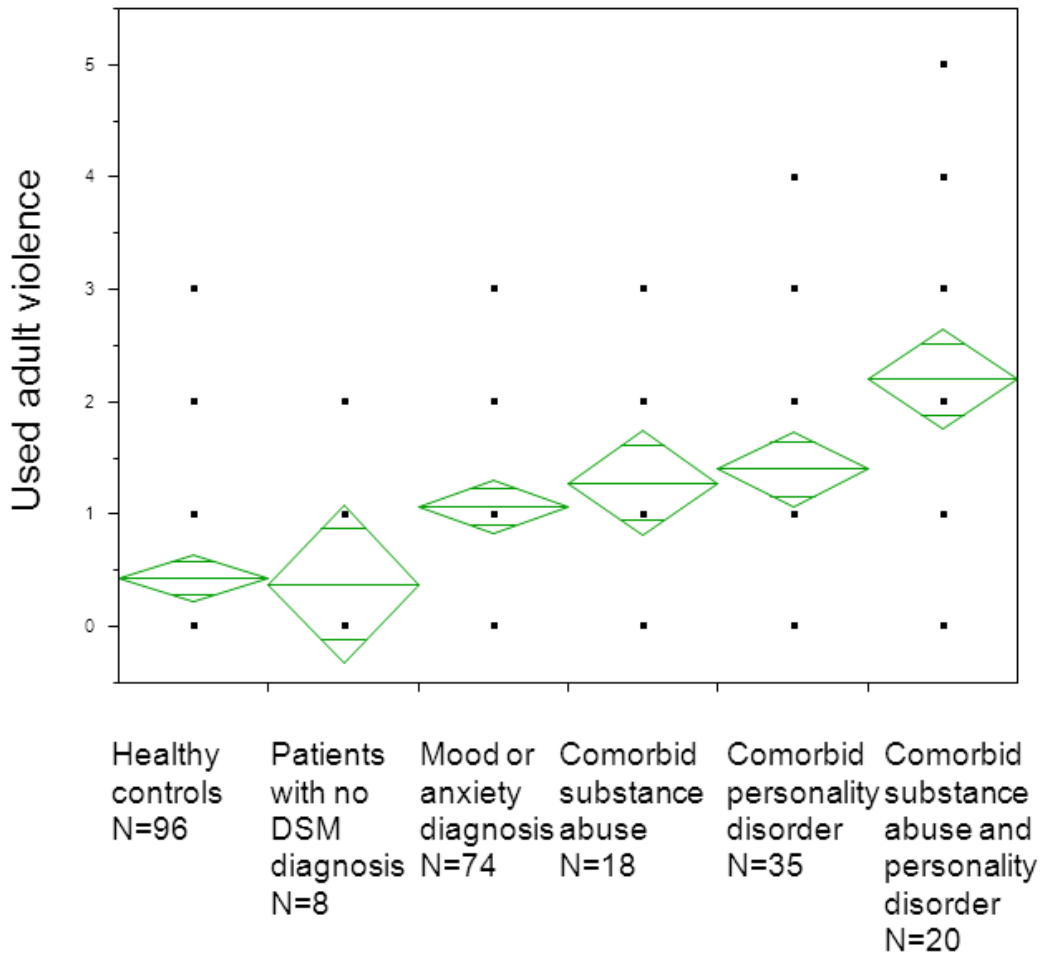

Figure 8. Levels of expressed interpersonal violence as an adult in healthy controls (n = 95) and in suicide attempters (n = 161), divided into groups with regard to DSM diagnoses.

Six patients were not diagnosed for Axis II disorders and were not included in the analysis. Diagnostic groups did not overlap. The upper, middle and lower vertical lines in the rhomboids show the mean and the standard error. The black squares show KIVS ratings represented in each sub-sample. Healthy controls differed from suicide attempters with Axis I or II diagnoses.

4.2.2 Childhood violence as a risk factor for adult violence

Expressed violence as a child was significantly correlated with adult interpersonal violence in suicide attempters (rho = 0.36, $p < 0.0001$). Exposure to violence as a child was also significantly correlated with use of adult violence by suicide attempters (rho = 0.28, p = 0.0003).

Male patients rated higher than female patients in Expressed violence as a child ($p < 0.0001$, Kruskal-Wallis). There were no gender differences in the ratings of Exposure to violence as a child or in use of violence as an adult among patients. Expressed violence as a child was significantly correlated with adult interpersonal violence in both male and female suicide attempters (rho = 0.47, $p < 0.0001$ and rho = 0.38, $p < 0.0001$, respectively). Exposure to violence as a child was also significantly correlated with adult interpersonal violence in both male and female suicide attempters (rho = 0.32, p = 0.01 and rho = 0.24, p = 0.02, respectively).

4.2.3 Regression analyses

A multivariate logistic regression analysis was performed with the two KIVS ratings, i.e., Expressed violence as a child and Exposure to violence as a child, together with a Substance Abuse diagnosis, Personality Disorder diagnosis and Age as predictors of adult interpersonal violence in suicide attempters. The regression model was significant (chi square = 45.6, DF = 5, $p < 0.0001$). Expressed violence as a child, Substance Abuse and Age were significant predictors of adult interpersonal violence. Table 4 shows odds ratios of clinical predictors of adult interpersonal violence. Broken down by gender, Personality Disorder predicted violence as an adult in male suicide attempters in Table 5.

Table 4. Predictors of violence as an adult in a sample of 161 suicide attempters. Multivariate logistic regression analysis was used.

	Adult Violence	
	Odds ratio (95% CI)	p-value
Expressed violence as a child	2.88 (1.54–6.03)	0.0009
Exposure to violence as a child	1.27 (0.82–1.99)	0.29
Substance Abuse diagnosis	10.93 (3.36–40.74)	< 0.0001
Personality Disorder diagnosis	2.47 (0.74–8.70)	0.14
Age	0.91 (0.84–0.97)	0.0016

Model fit: Chi-square = 45.6, DF = 5, $p < 0.0001$.

Table 5. Predictors of violence as an adult in female and male suicide attempters. Multivariate logistic regression analyses were used.

	Adult Violence			
	Females (n = 98)		**Males (n = 63)**	
	Odds ratio (95% CI)	*p*-value	Odds ratio (95% CI)	*p*-value
Expressed violence as a child	2.53 (0.84–8.27)	0.095	3.30 (1.16–13.10)	0.025
Exposure to violence as a child	1.26 (0.71–2.27)	0.42	1.60 (0.68–4.32)	0.28
Substance Abuse diagnosis (Yes vs No)	8.21 (1.66–49.85)	0.0096	22.05 (2.97–351.53)	0.0016
Personality Disorder diagnosis (Yes vs No)	1.02 (0.17-5.45)	0.98	13.94 (1.50-337.44)	0.018
Age	0.91 (0.82–0.98)	0.016	0.85 (0.70–0.97)	0.013

Female Model fit: Chi-square = 17.8, DF = 5, p = 0.0031. Male Model fit: Chi-square = 30.5, DF = 5, $p < 0.0001$.

4.2.4 Receiver operating characteristic analyses

When the KIVS subscale, Expressed violence as a child, was entered as a predictor of adult interpersonal violence among all the suicide attempters, an ROC analysis revealed an AUC of 0.79, a sensitivity of 100%, a specificity of 49% and an optimal cut-off of 1. On entering two predictors, i.e., Expressed violence as a child and Substance Abuse diagnosis on the same sample, the ROC analysis showed an AUC of 0.84, a sensitivity of 71% and a specificity of 89%. When the KIVS subscale, Expressed violence as a child, was entered as a predictor of adult interpersonal violence among male suicide attempters, an ROC analysis revealed an AUC of 0.81, a sensitivity of 64%, a specificity of 88% and an optimal cut-off of 2. On entering two predictors, i.e., Expressed violence as a child and Substance Abuse diagnosis for male suicide attempters, the ROC analysis gave an AUC of 0.86, a sensitivity of 81% and a specificity of 84%. When Expressed violence as a child on the KIVS subscale was entered as a predictor of adult interpersonal violence among female suicide attempters, an ROC analysis revealed an AUC of 0.78, a sensitivity of 100%, a specificity of 63% and an optimal cut-off of 1. Entering two predictors, i.e., Expressed violence as a child and a Substance Abuse diagnosis for the female suicide attempters, revealed an AUC of 0.83, a sensitivity of 100% and a specificity of 52%.

4.3 STUDY III

4.3.1 Patient characteristics and the CSF 5-HIAA concentrations

CSF 5-HIAA concentrations were normally distributed (Shapiro-Wilk test, $p < 0.2$) and did not significantly differ between men and women (87 ± 8.8 nM and 95 ± 6.6 nM, respectively; $p < 0.48$). CSF 5-HIAA concentrations were not significantly correlated with height or age ($p < 0.38$ and $p < 0.42$, respectively).

4.3.2 The CSF 5-HIAA concentrations and the expressed violent behaviour as a child and as an adult

CSF 5-HIAA concentrations were neither significantly correlated with Expressed violence as a child nor with Expressed violent behaviour as an adult measured with the KIVS.

4.3.3 The exposure to violence as a child and the psychopathology in suicide attempters

Patients with a current Personality Disorder diagnosis had significantly higher Exposure to violence as a child compared to patients without such a diagnosis ($Z = 2.9$, $p < 0.004$).

Exposure to violence as a child correlated significantly with Depression severity measured with MADRS (Spearman's rho = 0.40, $p = 0.01$).

4.3.4 CSF 5-HIAA concentrations and exposure to violence as a child

CSF 5-HIAA concentrations showed a trend to negative correlation with Exposure to violence as a child in the whole group of suicide attempters (Spearman's rho = − 0.26, p = 0.08). In women, but not in men, CSF 5-HIAA concentrations showed a significant negative correlation with the Exposure to violence as a child measured with the KIVS (Spearman's rho = − 0.49, p = 0.01), Figure 9.

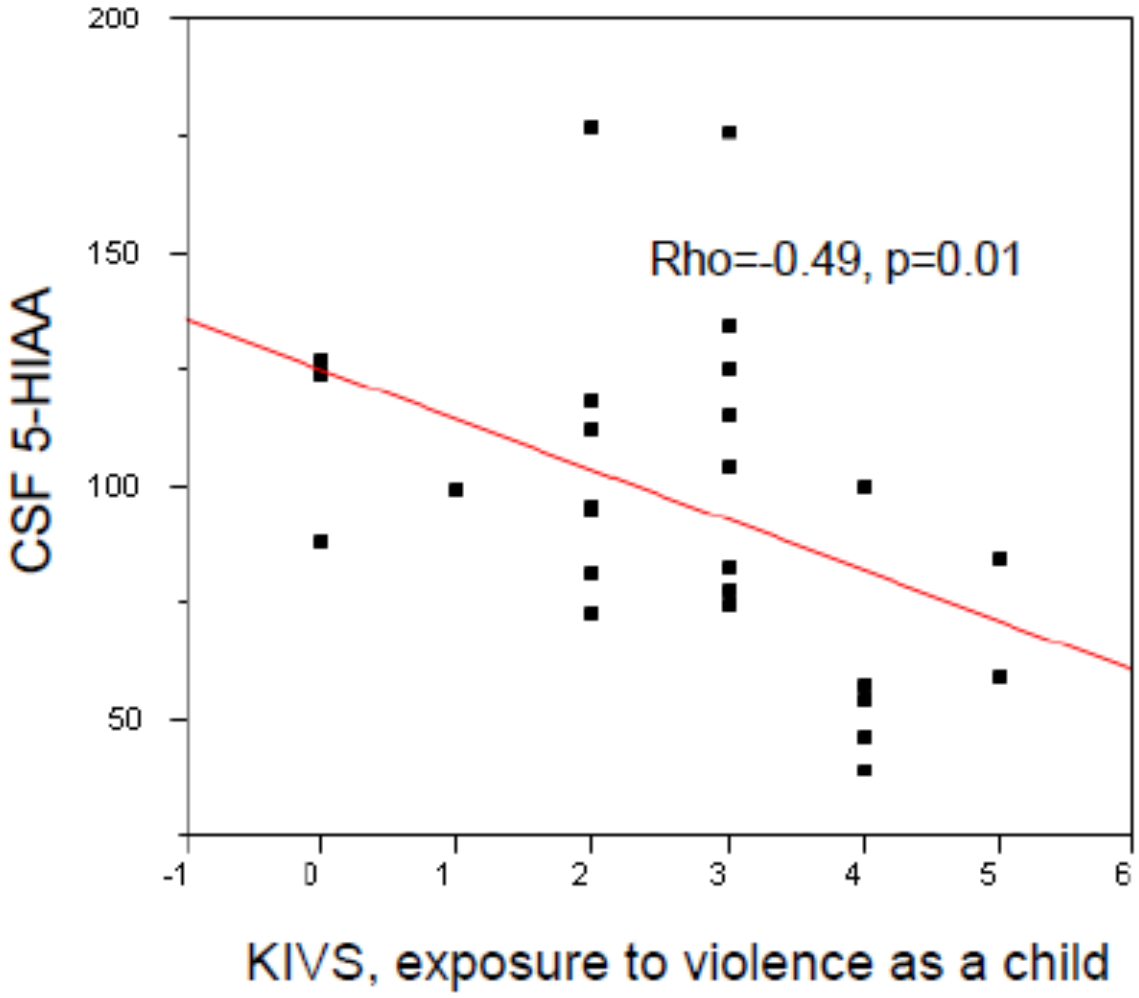

Figure 9. The correlation between exposure to violence as a child measured with the KIVS and the concentration of CSF 5-HIAA in female suicide attempters.

4.3.5 Exposure to violence as a child, CSF 5-HIAA concentrations and expressed violent behaviour as an adult

There was a correlation between Exposure to violence as a child and Expressed violent behaviour as an adult measured with the KIVS in the whole group of suicide attempters (Spearman's rho = 0.37, p = 0.02).

When CSF 5-HIAA concentrations was split by the median, there was a significant correlation between Exposure to violence as a child and Expressed violent behaviour as an adult in suicide attempters with concentrations below the median (Spearman's rho = 0.59, p = 0.006), whereas in suicide attempters with CSF 5-HIAA concentrations above the median Exposure to violence as a child did not correlate with Expressed violent behaviour as an adult (Spearman's rho = 0.07, p = 0.8), Figures 10 and 11.

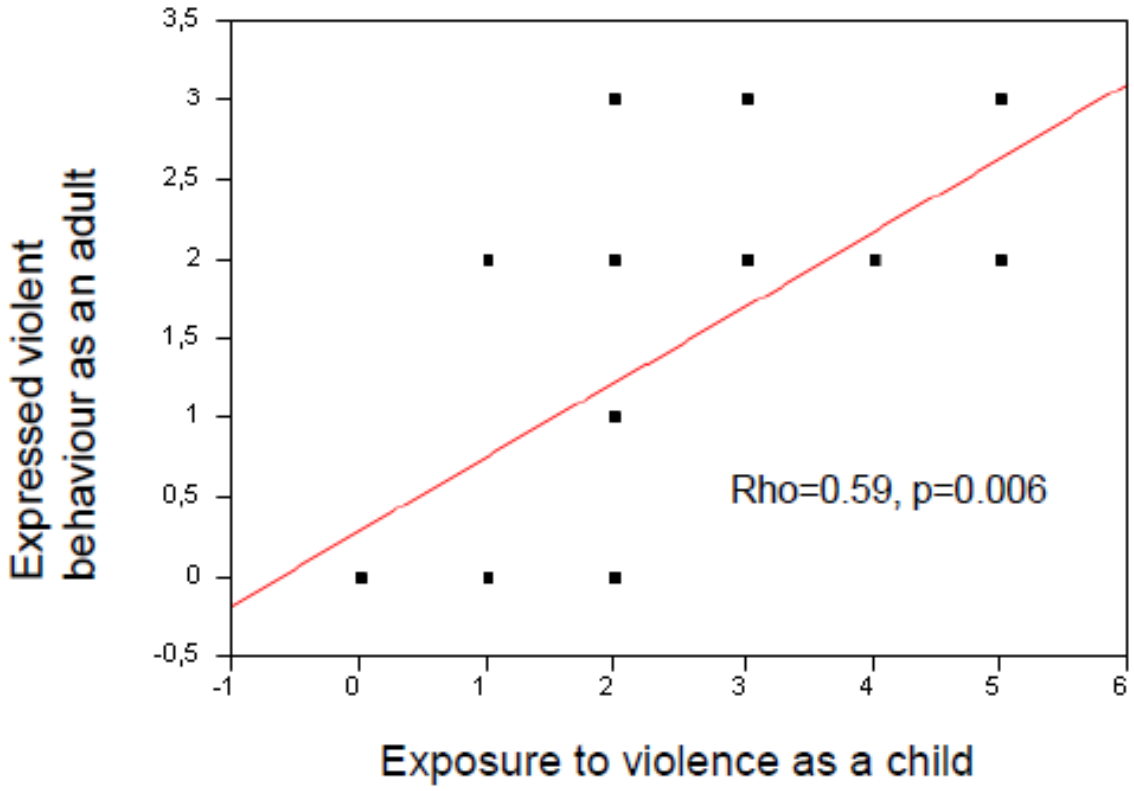

Figure 10. The correlation between exposure to violence as a child and expressed violent behaviour as an adult in suicide attempters with CSF 5-HIAA concentrations below the median.

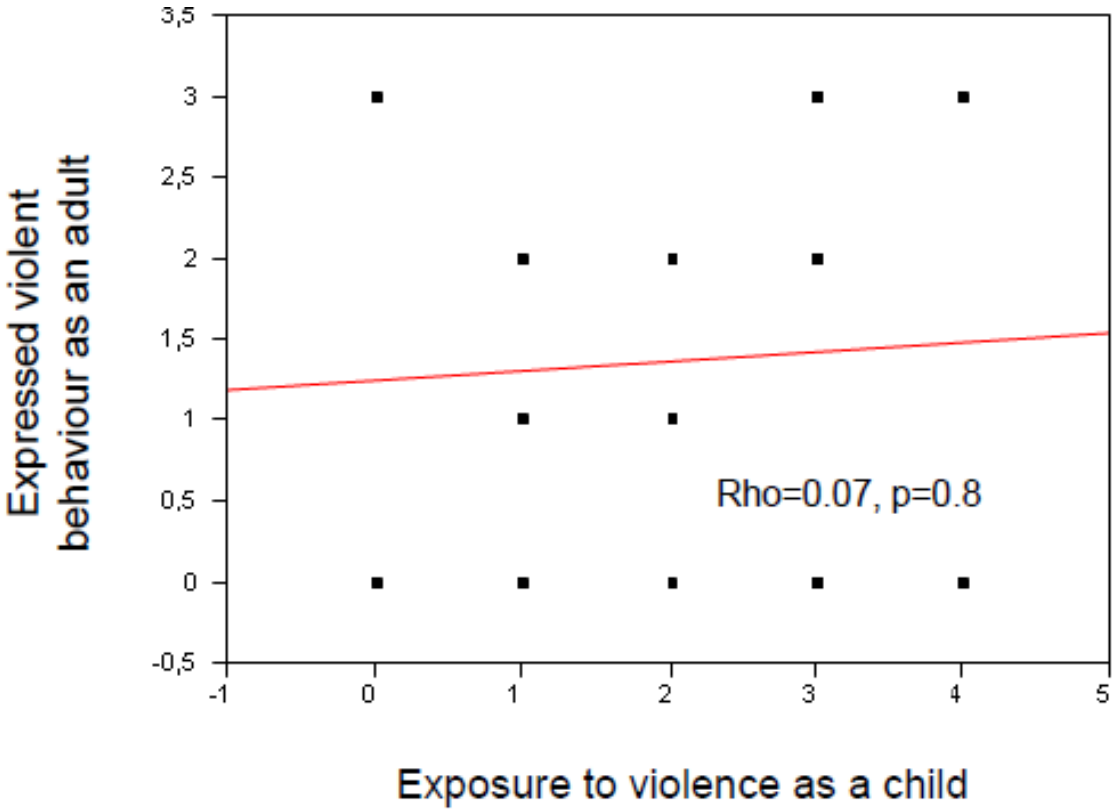

Figure 11. The correlation between exposure to violence as a child and expressed violent behaviour as an adult in suicide attempters with CSF 5-HIAA concentrations above the median.

The correlation coefficients for Exposure to violence as a child and Expressed violent behaviour as an adult differed significantly between suicide attempters with CSF 5-HIAA concentrations above and below the median ($p < 0.03$).

4.4 STUDY IV

4.4.1 Mortality and the causes of death among violent offending men

In the total cohort of 48,834 Swedish conscripts, 2,671 (5.5%) died during the follow-up period at an average age of 42 years. Violent offenders died at an average age of 41.8 years. Violent offenders (n = 2,374) had a total mortality of 13.7 % during the follow-up period, compared to 5.0 % in the other conscripts (Table 6).

Table 6. Underlying causes of death among violent offenders among 48,834 Swedish conscripts

	Violent offenders N = 2,374		**Others N = 46,460**	
	Death cases n = 326		Death cases n = 2,345	
	n	%	n	%
Accidents	37	11.3	383	16.3
Undetermined suicide	14	4.3	48	2.0
Completed suicide	49	15.0	376	16.0
Alcohol-related	115	35.3	340	14.5
Drug-related	18	5.5	34	1.4
Circulatory disease	41	12.6	359	15.3
Neoplasm	31	9.5	529	22.6
Other causes	21	6.4	276	11.8

In the violent offender group the most frequent underlying or contributing cause of death, 35.3 %, was alcohol-related, compared to 14.5 % among other conscripts. Mortality due to undetermined or completed suicide was higher in the violent offender group (2.7 %) than in the other conscripts (0.9 %).

4.4.2 Bivariate and multivariate analyses

The bivariate analyses showed that the recidivists with respect to violent convictions had a nearly eleven times higher hazard of dying due to an alcohol- or drug-related cause and a nearly four times higher hazard of suicide compared to the other conscripts (Table 7).

Table 7. Mortality and underlying causes of death among offenders convicted for one violent crime or two or more violent crimes in a cohort of 48,834 Swedish conscripts. Cox proportional bivariate analyses were used. Hazard ratios (HRs) and 95% confidence intervals (95% CIs) are given with regard to all living subjects.* Victims of violent crime (n = 500) and individuals who were both offenders and victims (n = 235) were not included in the analyses.

	1 violent conviction (n = 1,458) *HR (95% CI)*	**2+ violent convictions** (n = 681) *HR (95% CI)*
Accidents	1.75 (1.13–2.72)	2.21 (1.25–3.93)
Suicide	2.03 (1.35–3.07)	3.59 (2.26–5.69)
Alcohol and drugs	4.28 (3.21–5.72)	10.84 (8.23–14.28)
Circulatory disease	1.89 (1.21–2.93)	2.68 (1.54–4.66)
Neoplasm	1.05 (0.65–1.70)	1.55 (0.86–2.82)
Other causes	0.81 (0.38–1.71)	1.57 (0.70–3.53)
All causes	1.98 (1.68–2.34)	3.94 (3.30–4.70)

*Cases of death due to accidents, suicide, neoplasm, circulatory disease, and other causes in combination with Alcohol- or Drug-Related diagnoses were excluded.

Multivariate analyses showed that violent recidivists had a more than threefold higher hazard of dying in connection with an Alcohol- or Drug-Related diagnosis and a twofold higher hazard of dying from suicide, while no significant risk was found for accidents, neoplasm, circulatory disease and other causes (Table 8).

Table 8. Adjusted* mortality and underlying causes of death among offenders convicted for one violent crime or two or more violent crimes in a cohort of 48,834 Swedish conscripts. Cox proportional multivariate analyses were used. Hazard ratios (HRs) with 95% confidence intervals (95% CIs) are given in relation to all living subjects.** Victims of violent crime (n = 500) and individuals who were both offenders and victims (n = 235) were not included in the analyses.

	1 violent offence (n = 1,458) *HR (95% CI)*	**2+ violent offences** (n = 681) *HR (95% CI)*
Accidents	1.26 (0.80–2.00)	1.09 (0.57–2.09)
Suicide	1.55 (1.02–2.35)	2.39 (1.51–3.77)
Alcohol and drugs	2.04 (1.49–2.80)	3.03 (2.20–4.17)
Circulatory disease	1.48 (0.92–2.38)	1.80 (0.99–3.28)
Neoplasm	0.89 (0.52–1.52)	1.47 (0.79–2.74)
Other causes	0.49 (0.20–1.20)	0.85 (0.32–2.12)
All causes	1.39 (1.16–1.66)	2.01 (1.64–2.46)

*Adjusted for the variables Psychiatric diagnosis at conscription, Emotional control, Social maturity, Divorced parents, Contact with the police or child welfare section of a municipal welfare committee, Lowered marks due to misconduct at school, Ever run away from home, Smoking, Problem drinking and Drug misuse.

**Cases of death due to accidents, suicide, circulatory disease, neoplasm, and other causes in combination with Alcohol- or Drug-Related diagnoses were excluded.

4.4.3 Stratification for alcohol, drug and psychiatric inpatient care

In Table 9, we stratified for alcohol, drug misuse and psychiatric inpatient care during the follow-up period. Violent offenders with Alcohol- or Drug-Related diagnoses had nearly a fourfold higher hazard of dying compared to violent offenders with no such diagnoses. The hazards were much higher compared with all other participants: HR = 5.53 and HR = 7.67, respectively.

With regard to mortality due to suicide, we also controlled for inpatient care. We found that especially repeated violent offense were associated with higher hazards of suicide, with HRs of 1.94 (95% CI 1.33-2.82) and 1.71 (95% CI 1.14-2.58) when controlled for psychiatric inpatient care alone and psychiatric inpatient care in combination with inpatient care for alcohol and substance misuse, respectively (not shown in tables).

Table 9. Mortality among violent offenders stratified for hospitalization with an Alcohol- or Drug-Related diagnosis or a psychiatric diagnosis. Bivariate analyses using Cox proportional regression. Hazard ratios (HRs) are given with 95% confidence intervals (95% CIs). Victims of violent crime (n = 500) and individuals who were both offenders and victims (n = 235) were not included in the analyses. (*psychiatric = psychiatric diagnosis)

Inpatient care	**Mortality** *HR (95% CI)*
Violent convictions + **alcohol** vs violence only	3.75 (2.96–4.78)
Violent convictions + **drugs** vs violence only	3.91 (2.99–5.11)
Violent convictions + **psychiatric*** vs violence only	2.54 (1.99–3.23)
Violent convictions + **alcohol** vs others	5.53 (4.70–6.50)
Violent convictions + **drugs** vs others	7.67 (6.08–9.68)
Violent convictions + **psychiatric*** vs others	4.81 (3.97–5.83)

5 DISCUSSION

There was an association between a diagnosis of Psychosis and convictions for violent crime in the bivariate analysis in Study I. However, individuals meeting the diagnostic criteria for Psychosis were relatively few and there was no significant association with violent convictions in the preliminary multivariate analyses and therefore the group was not included in the final multivariate analyses. There seemed, however, to be a tendency to association between Psychosis and violent crime in the preliminary multivariate analyses, but the association might have been masked by markedly spread confidence intervals, thus making the relationship non-statistically significant. The result could be interpreted as there possibly being an association, but the number of persons meeting the diagnostic criteria for Psychosis was too small for an adequate comparison with much larger groups of conscripts without the diagnosis. It has also been shown by other authors in previous studies that only a minority of the individuals who eventually developed Psychosis had manifested psychotic symptoms at the time of conscription [80]. Even though violent crimes also often occur before an individual can be diagnosed with psychosis [81, 82], the presence of violent offending in Psychosis is most probably underestimated in our study. An alternative interpretation of these results is that the possible association between Psychosis at conscription and violent offending later in life does not exist or is due to other factors, such as personality pathology or Substance Abuse co-morbidity in line with what has been suggested in reviews [24, 83]. Unfortunately, Schizophrenia Spectrum Psychosis was an exclusion criterion in Studies II and III. Therefore we could not further investigate the association between Psychosis and interpersonal violence.

In summary, Study I found no evidence for an association between Psychosis and violent offending, but a possible association cannot be ruled out based on our results.

Affective and Anxiety Disorders among men, clustered together in a single group according to the neuroses concept in Study I, were associated with a conviction for violent crime, but, to a large extent, the association could be explained by other factors. Nevertheless, Affective and Anxiety Disorders diagnosed at conscription still remained a weak, but significant, predictor of a future conviction for violent crime, also after adjusting for various potential confounders. This result is in line with what other authors have reported [84, 85]. A recent study has also demonstrated a relationship between Depression and violent crime [86]. When interpreting our results, one must take into account that we clustered together different subgroups of Affective Disorders. An earlier study has demonstrated considerable heterogeneity in the affective group with a higher criminality rate in patients with Bipolar Disorder and patients suffering from Unipolar Minor or Intermittent Depression, whereas no increased criminality was observed in patients with Unipolar Major Depression [87]. However, the diagnostic procedure during the years 1969–1970, according to ICD-8, categorized Bipolar Disorder as a Psychotic Syndrome when manifested as an Affective Psychosis, Manic or Depressed type. On the other hand, some depressed conscripts may have

had a masked Bipolar Disorder that had not yet developed into a manic episode. Affective Disorders are also common conditions, often having an onset later in life and therefore could not be included in our analyses. Even with all these biases in mind, our interpretation of the results is that there is a plausible association between Affective and Anxiety Disorders and violent crime in men. The majority of the included patients in Studies II and III were diagnosed with an Affective Disorder, which made it difficult to further investigate the relationship.

A Personality Disorder diagnosis in men was associated with interpersonal violence and was an independent predictor of adult interpersonal violence in both Study I and Study II. In our statistical analyses, we handled the Personality Disorders as a single category because a Personality Disorder Not Otherwise specified and Other Personality Disorders accounted for most individuals in the group. There was no association between a Personality Disorder diagnosis and interpersonal violence among women in Study II. It was not possible to investigate this matter in Study I because the conscript cohort did not contain women.
On performing sensitivity analyses in Study I, we found that the association between Personality Disorders and convictions for violent crime could not be explained by a high proportion of individuals with an Antisocial Personality Disorder. This is in accord with a large-scale review which showed that all Personality Disorders evinced an increase in the risk for violent crimes when individuals with a Personality Disorder were compared with general population controls [88]. The association between Personality Disorders and conviction for violent crime in study I also remained significant after adjusting for factors that reflect early behavioural problems. In fact, variables assessing deviant behaviour were often connected with Personality Disorders.

In Study II, a high proportion of the male suicide attempters were diagnosed with a Borderline Personality Disorder with a co-morbid Antisocial Personality Disorder, where the latter diagnosis in a sensitivity analysis could explain the association between Personality Disorders and the use of adult violence by men. This has been described earlier when studying cohorts of psychiatric patients with a Borderline Personality Disorder [36-38]. In study II, we could not find an association between Personality Disorders and interpersonal violence among women, probably due to the fact that virtually no female suicide attempter was diagnosed with an Antisocial Personality Disorder.

Substance-related Disorders were associated with a significantly increased risk of interpersonal violence as an adult in both men and women in Studies I and II. This result is in line with what other studies have shown in large population-based cohorts [39, 89] and in cohorts with Affective Disorders [29, 85, 90, 91]. In Study I, the results were robust after adjusting for potential confounders, some of them corresponding to antisocial personality traits. The design of Study I, with an investigation of a birth cohort, also prevented enrichment of antisocial traits through a selection bias and allowed us to make a realistic estimation of the extent to which the Substance-Related Disorder *per se* is a predictor of violent crime. On the other hand, in the cohort in Study I, Substance-Related Disorders consisted mainly of Drug Dependence (67%), i.e., dependency on illegal substances

connected with a high acceptance of anti-social acts. In reality, however, Alcoholism is far more prevalent in the Swedish citizenry and it could be speculated whether a truer representation (better detection) of substance use problems in the cohort would alter the findings and, if so, in what direction.

When Substance Abuse in Study II occurred together with a Mood or Anxiety Disorder and a co-morbid Personality Disorder, the significantly increased risk of violence as an adult because of Substance Abuse appeared to be further enhanced by this combination of Personality Disorder and Substance Abuse. Borderline Personality Disorder was common in Study II and our finding is supported by previous reports that Borderline Personality Disorder with co-morbid Substance Abuse elevates the risk for violence [33, 38].

Thus, to summarize our results in Study I and II regarding Substance Abuse and the risk of interpersonal violence: Substance Abuse *per se* is an independent predictor of interpersonal violence in adults, but the significantly increased risk for violence is particularly reinforced if the Substance Abuse Disorder is combined with a Personality Disorder.

The diagnosis Mental Retardation was included in Study I, but could not be investigated in Studies II and III because it was an exclusion criterion there. In Study I, men with a diagnosis of Mental Retardation at conscription had the highest risk of a future conviction for violent crime, taking into account other early risk factors. This result is in line with longitudinal studies showing that low-level intelligence is a significant risk factor for offending [45, 92-94]. In our study, Mental Retardation had a stronger association with convictions for violent crime than Personality Disorders and Substance-Related Disorders. When interpreting our results it should be noted that the military authorities had already excluded individuals considered not to be fit for military service before conscription. Among others, this eliminated group also included individuals with more severe forms of Mental Retardation requiring support from health and social services. In the present study, we also chose to include individuals diagnosed with Borderline Mental Retardation (intelligence quotient 70–85) as mentally retarded because this group is well represented in clinical populations exposed to violence risk assessments. Other researchers have also called attention to this group's inclusion in earlier studies on criminal careers [46]. In Study I, we had information on confounding factors considered relevant in a risk assessment perspective, thus enabling adjustments for different behavioural variables most likely not to be linked to Mental Retardation *per se*, but, instead, indicating a more general propensity towards anti-social behaviour/attitudes due to other conditions or circumstances. Poor coping skills due to Mental Retardation may sometimes be misinterpreted to be an anti-social behaviour caused by a Conduct Disorder.

Our result indicating that Mental Retardation carried the highest risk for a future conviction for violent crime is not reflected in any of the examined violence risk assessment instruments, which do not directly take into account Mental Retardation as a diagnosis, but, instead, several of the other psychiatric diagnoses or risk factors. Based on our findings, we suggest considering inclusion of Mental Retardation in future revisions of the violence risk assessment instruments. Individuals with an early onset of violent crime should, in

appropriate cases, also undergo a thorough neuropsychiatric investigation to determine whether there is masked Mental Retardation. The earlier the detection, the better the basis there is for planning appropriate support adjusted to the Mental Retardation, which may lead to a lower risk of violence.

There was no association between Neurological Disorders and violent convictions in Study I, indicating that they are not predictors of convictions for violent crime in men. Neurological Disorders were not investigated in the other studies in this thesis. The lack of association in Study I might be explained by the fact that the majority of the subjects with neurological conditions in the studied cohort consisted of conscripts with diagnosed Epilepsy (n = 143 of 189), thus replicating previous studies in which no association could be found between Epilepsy and violent crimes [95]. It is not possible to know how the association would have been if more conscripts had been included with other neurological diagnoses than Epilepsy: for instance, diagnoses equivalent to traumatic brain injury, Mental Disorders Associated With Brain Trauma or Mental Retardation Following Trauma, which occurred only in a few cases. This might be due to the fact that the threshold at conscription for diagnosing these conditions was high. It is more likely, however, that the persons in the source population with these conditions had already been excluded by the military authorities prior to enrolment and therefore could not be included in the study population. Consequently, the lack of association between Neurological Disorders and violent convictions applies only to the diagnosis of Epilepsy.

Early behavioural problems were important predictors of interpersonal violence in Studies I and II in this thesis, which is in line with previous research [54, 96]. Previous studies have also shown that a history of any violent act and juvenile detention or a diagnosis of Conduct Disorder before age 15 predicted violent behaviour, even in relation to co-occurring severe mental illness and substance use [26, 55]. In Study I, early behaviour problems had, besides mental disorders, the strongest association with convictions for violent crime in adulthood in men. In particular, the variable Contact with the police or child welfare committee and also Lowered marks due to misconduct at school were associated with a future conviction for violent crime. The self-reported information in this context reflects an expression of some type of aggressive behaviour or similar misbehaviour during childhood or adolescence. In Study II, early behavioural problems were measured on one of the subscales in KIVS and it was found that, in the whole group of suicide attempters, the scores on ‘Expressed violence as a child’ were significantly correlated with adult interpersonal violence and the self-reported use of violence in childhood assessed by a structured rating was also a significant independent predictor of adult interpersonal violence. Female patients rated lower than males, however, on the KIVS subscale, Expressed violence as a child. This is probably the reason why this variable was not a significant independent predictor of adult interpersonal violence in women, even though it still correlated significantly with violence as an adult in women. ROC analyses also showed that there was a lower optimal cut-off for `Expressed violence as a child´ in females than in male suicide attempters. An ROC analysis of the prediction model for adult violence on the KIVS subscale, Expressed violence as a child,

gave an acceptable to good discrimination. Using two predictors, Expressed violence as a child and Substance Abuse diagnosis, gave good discrimination.

In summary, the main finding still remains robust, i.e., violent behaviour in childhood is a predictor of adult interpersonal violence. We suggest that violent behaviour in childhood should be measured in a structured way in violence risk assessments in psychiatric clinics and if combined with the variable Substance Abuse, it results in an even better prediction of adult interpersonal violence.

In the birth cohort of men included at conscription in Study I, there was a weak association between childhood maltreatment and interpersonal violence among men. In Study III, there was a weak correlation between the exposure to violence as a child and the expressed violent behaviour as an adult in the whole group of suicide attempters, giving some support to the 'cycle of violence' hypothesis along with previous studies [58, 97]. However, in the cohort of suicide attempters in Study II, exposure to violence as a child did not predict violence as an adult in multivariate logistic regression analyses. The literature contains some contradictory results. Findings from a cohort study indicated that those who had been abused or neglected as a child had an increased risk of delinquency, adult criminal behaviour and violent criminal behaviour [58]. Another study reported an association between having been bullied in childhood and aggressive behaviour in adulthood [98]. Other studies showed no association, however, between poor treatment from 10 to 12 years of age and non-violent or violent crimes between 12 and 24 years of age [60] or could not find any connection between the rougher forms of maltreatment during childhood and arrests in early adulthood [99]. One possible explanation for these inconsistent results in the literature and in Studies I–III is that childhood maltreatment may cause different trajectories in cohorts with different characteristics. This might be illustrated in Study III, where the variable, 'Exposure to violence as a child', was significantly correlated with Depression severity, measured with MADRS in suicide attempters. Thus, patients with high exposure to interpersonal violence as a child had more severe Depression, indicating that childhood trauma contributes to the severity and chronicity of Depression, as previously reported [100]. Patients with a Personality Disorder diagnosis in the suicide attempt cohort also had significantly higher scores on 'Exposure to violence as a child' compared to patients without such a diagnosis. The single most common Personality Disorder diagnosis in Study III was Borderline Personality Disorder, and the result is consistent with the literature on childhood trauma as a causative factor in the development of this Personality Disorder (for a review, see [101]), leading to more self-destructive aggression than interpersonal violence directed towards other individuals. Another explanation for the contradictory results in Studies I–III is that a biological mechanism in the serotonergic activity might be involved. This serotonergic mechanism is discussed in the next sections and may lead to inconsistent results regarding the effect of childhood maltreatment on adult interpersonal violence depending on the selection, composition and size of the studied cohorts.

In summary, child maltreatment is a possible predictor of adult interpersonal violence.

Exposure to stress early in life has an effect on the serotonergic system, a behavioural inhibitory system that has a modulating role regarding impulsivity and aggression. In Study III, we assessed the relationship between CSF 5-HIAA and Exposure to violence during childhood in suicide attempters. In the whole group of suicide attempters, CSF 5-HIAA showed a trend towards a negative correlation with Exposure to violence as a child. In women, but not in men, this negative correlation was significant. Physical or psychological adversity in childhood is associated with persistent serotonergic abnormalities in animal models and in humans. In primates, stressful rearing conditions are associated with altered CSF concentrations of 5-HIAA [102-104]. In humans, childhood neglect in males was shown to correlate negatively with CSF 5-HIAA concentrations [66]. Our results are partly in line with this report. The reason for the gender difference in Study III might reflect lack of statistical power; there were too few males (n = 15, compared to females, n = 27) to get a result that was statistically significant. Another explanation is that females seem to be more sensitive to exposure to violence during childhood. An increasing number of reports suggest a substantial influence of gender on the function of the serotonin system in experimental animal studies (see review by Veenema [105]), in serotonin-associated human psychiatric conditions, such as Depression [106-108] and in a human positron emission tomography (PET) study [109].

Our finding suggests that exposure to interpersonal violence during childhood may be associated with long-term alterations in the serotonin system and that there might be a gender difference in vulnerability.

In Study III on suicide attempters, we investigated the effect of the serotonergic system on violent behaviour. The CSF 5-HIAA levels did not correlate with expressed violent behaviour as an adult or as a child. This result contrasted with earlier studies on military personnel with Personality Disorders, which found a significant negative correlation between CSF 5-HIAA and lifetime aggressive behaviour [61]. Lower concentrations of CSF 5-HIAA have been reported subsequently for impulsive murderers [63] and arsonists [110]. However, other studies have reported no negative correlation between CSF 5-HIAA and measures of violence [111] or a positive correlation between CSF 5-HIAA and a composite measure of impulsive aggression [112-114]. The absence of a correlation between CSF 5-HIAA and expressed violent behaviour as an adult in Study III might be due to different patient characteristics compared with samples in some of the earlier studies. For instance, none of the suicide attempters in Study III scored at the two highest levels of expressed violent behaviour on the KIVS subscale as an adult. Studies reporting the absence of a negative correlation or the presence of a positive correlation between CSF 5- HIAA and aggression largely include subjects who are not as severely aggressive as those in studies that report negative correlations [114].

In a further step in Study III, we studied the effect of the serotonergic system on violent behaviour in even more detail by using the median split of CSF 5-HIAA. Exposure to violence as a child then showed a significant positive correlation with expressed violent behaviour as an adult only in suicide attempters with CSF 5-HIAA below the median. In

suicide attempters with CSF 5-HIAA above the median, the Exposure to violence as a child did not correlate with expressed violent behaviour as an adult. This suggests that suicide attempters with low concentrations of CSF 5-HIAA and who have been exposed to violence in childhood have a more pronounced aggression dyscontrol as adults, whereas suicide attempters with high concentrations of CSF 5-HIAA may not have this inclination to use violence as adults if exposed to violence as children. This adds to the evidence that alterations in the serotonergic system, with resulting in lower concentrations of 5-HIAA, lead to impaired aggression control in adulthood and can be considered, together with impulsivity-aggressivity, to be an intermediate phenotype of suicidal and violent behaviour and thus a mediator of the risk of violence. Early traumatization is generally regarded as a causal or mediating risk factor for aggressive and violent behaviour [115]. Our result in Study III is supported by an earlier study on maltreated children who were genotyped for a functional polymorphism in the neurotransmitter-metabolizing enzyme monoamine oxidase A (MAOA), which metabolizes serotonin to 5-HIAA. This *MAOA* polymorphism has been shown to be associated with CSF 5-HIAA concentrations in healthy individuals [116]. Children with high levels of the *MAOA* alleles associated with high expression were less likely to develop antisocial problems, whereas children with alleles predicting low MAOA activity had a higher composite index of antisocial behaviour [117].

In the Cox proportional bivariate and multivariate analyses in Study IV, we found that violent recidivists had a significantly higher hazard of dying from an Alcohol or Drug-Related diagnosis and higher hazards of dying from suicide, while no significant risk was found for other causes of death. Other researchers have demonstrated similar associations [118]. After stratification in Study IV, it was shown that violent offenders who had been treated in hospital for alcohol, drug or psychiatric diagnoses had a significantly higher hazard of dying compared to violent offenders with no such diagnoses. Our findings are not at all surprising, since Studies I–II showed that exactly the same risk factors that increased the risk for an overall mortality, i.e. dependence diagnoses and psychiatric conditions, also increased the risk for violent behaviour in conscripts and suicide attempters. Therefore, one might suspect that the higher mortality among violent offenders is not a consequence of the violence *per se*, but is caused by the background conditions. Support for this interpretation is found in a study, that examined nationwide 5-year consecutive cohorts of individuals admitted to hospital for mental disorders in Denmark, Finland and Sweden. Individuals admitted to hospital for a mental disorder had a higher mortality than that of the general population in all three countries studied and the life span of the men with mental disorders was 20 years shorter and that of women 15 years shorter than that of the general population [119]. On taking this into consideration and adjusting for dependence diagnoses and psychiatric conditions as confounders in the Cox proportional multivariate model, it becomes clear that something closely connected with the violent behaviour other than these confounding diagnoses and the violence *per se* was responsible for the association of violet behaviour with a higher mortality. A population-based cohort study of Swedish homicide offenders, who were followed for a minimum of 22 years and investigated using survival analysis, exemplified this

by demonstrating a clear and straightforward connection between violent behaviour and mortality. In the studied cohort, the suicides constituted the major portion, 30%, of the mortality. A high percentage of the suicides (72%) occurred early, within 2 years after the homicide, but the increased risk of committing suicide persisted throughout life in the cohort. The researchers concluded that the violent behaviour resulting in homicide is a strong predictor of future suicide, and similar biological mechanisms may be involved in violent criminality and suicidal behaviour [120]. The biological mechanism here might be reduced serotonergic activity, leading to behavioural dysregulation, as shown in Study III.

In a wider perspective in the public debate, but also in clinical practice when making risk assessments for violence, it should be emphasized that such assessments are not only of value for the public regarding protection from the perpetrator. They are also as a tool for identifying violent offenders who are at high risk of mortality and thereby giving this group a better chance to survive from Alcohol- or Drug-Related conditions or suicide by providing proper support and treatment for the underlying conditions.

The strengths and limitations of the different studies were closely related to the size of the cohorts. In the conscription cohorts in Studies I and IV, many individuals were included, but the diagnostic procedure was based on clinical assessments and thus were not as thorough and detailed as in the smaller cohort with suicide attempters in Studies II and III, which used standardized diagnostic procedures for a specified and accurate diagnosis. A larger number of included individuals would have been preferable in these studies for a better statistical precision.

The strengths of Studies I and IV include the fact that the conscripts were from a large birth cohort recruited nationwide with a coverage of 97%–98%, who were thoroughly examined during two days by psychologists, physicians and, if necessary, psychiatrists, in a procedure that included cognitive tests. Furthermore, the studied outcomes, conviction for violent crime after conscription and mortality, were obtained from national registers covering a period of more than 35 years, namely, the National Crime Register and the Cause of Death Register with a drop-out rate estimated to be less than 1% [121, 122], as well as the National Inpatient Register from which information was obtained on treatment at hospitals [123]. The strength of Studies II and III included diagnoses based on semi-structured SCID interviews and expressed violence measures obtained from structured interviews. Study III also included biological data.

A limitation in Studies I and IV was that women were exempted from conscription at that time, which restrains the generalizability of the findings of psychiatric diagnoses and future convictions for violent crime to men only. Furthermore, we had no information about Attention Deficit Hyperactivity Disorder, Autism and too few subjects with traumatic brain injury to analyse these conditions. In these studies, the category violent crime conviction was based on the Swedish Penal Code categorization of violent crime. Sex crimes and robbery were not included in the category, which can be regarded as a limitation. Information about crimes that had not come to the attention of the police was lacking. Use of non-anonymous

questionnaires may have resulted in lower reporting of sensitive issues than may have been elicited with anonymous questionnaires. Some of the men with psychiatric disorders probably were not conscripted and we could only focus on those with a relatively early onset of psychiatric and neurological disorders. Thus, the sample does not represent the entire male population with these disorders.

The limitations in Studies II and III were the cross-sectional designs, which prevent causal interpretations of the relationships. Furthermore, the sample sizes were rather small, especially with regard to some of the diagnostic subgroups, and consisted only of suicide attempters. Another limitation was the absence of patients with Intravenous Drug Abuse, Schizophrenia and Mental Retardation, which were exclusion criteria, and which means that it was not possible to study these diagnoses, and the results are not generalizable to these groups of patients. All the information about expressed violent behaviour was obtained from interviews, and not registers, with a risk of introducing a recall bias regarding use of violence in childhood.

6 CONCLUSIONS

Mental disorders led to a general increase in the risk for interpersonal violence. Mental Retardation, Substance-Related Disorders and early behavioural problems, including violent behaviour in childhood, were important predictors of expressed interpersonal violence in adults. Personality Disorder was a predictor of expressed interpersonal violence in men. Affective-Anxiety Disorders and childhood maltreatment were weak predictors of adult interpersonal violence. Psychosis and Epilepsy were not predictors of violent offending.

Violence risk assessments on an advanced level should include a thorough psychiatric and psychological evaluation, including cognitive tests and information about early behavioural problems and childhood maltreatment. Poor coping skills due to Mental Retardation may sometimes be misinterpreted to be an anti-social behaviour caused by a Conduct Disorder. Individuals with an early onset of violent behaviour should, in appropriate cases, undergo a thorough neuropsychiatric investigation to determine whether there is masked Mental Retardation. The earlier the detection, the better the basis there is for planning appropriate support adjusted to the Mental Retardation, which may lead to a lower risk of violence. Based on our findings, we suggest considering inclusion of Mental Retardation in future revisions of the violence risk assessment instruments. Violent risk assessments on a basic level in clinical practice should include measurements of Substance Abuse and earlier violent behaviour in a structured way.

Exposure to interpersonal violence early in life had an effect on the serotonergic system, a behavioural inhibitory system that has a modulating role regarding impulsivity and aggression. This, in turn, led to aggression dyscontrol in a subgroup of traumatized individuals with a genetically determined low turnover of serotonin in the central nervous system. Childhood maltreatment was shown to be a weak predictor of adult interpersonal violence, but it might have also caused a different trajectory leading to more self-destructive aggression instead of expressed violence directed towards other individuals.

Violent recidivists had a significantly higher hazard of dying from an Alcohol or Drug-Related diagnosis and from suicide, but no significantly higher risk of dying from other causes. Thus, it was not the violence *per se,* but exactly the same risk factors that increased the risk of violent behaviour, i.e., dependence diagnoses and psychiatric conditions, that caused the higher overall mortality. The biological mechanism involving reduced serotonergic activity and leading to behavioural dysregulation might have also been involved, especially with regard to suicide mortality.

A risk assessment for violence is not only of value for the public regarding protection from the perpetrators, but is also a tool for identifying violent offenders who are at high risk of mortality, Thus, it may be possible to reduce the risk of interpersonal violence and to give this group a better chance to survive from Alcohol- or Drug-Related conditions or suicide by offering proper support and treatment for the underlying conditions.

7 FUTURE PERSPECTIVES

The overall objective in this thesis was to study common mental disorders and the associated risks for interpersonal violence, how other additional early risk factors may affect the risk of violence and to study the mortality among the users of violence. Other additional early risk factors included biological risk factors and, in this thesis, we focused on the monoamine serotonin in the serotonergic system. The studied cohort with information on the major serotonergic metabolite was, however, comparatively small, only 42 highly selected patients who have tried to commit suicide. A small sample size in selected cohorts is a common feature in many other earlier studies on biological risk factors for violence.

We have obtained approval from the Regional Ethical Review Board in Stockholm (Dnr 2010/468-31/3) to perform a larger study named 'Biomarkers of Violence Risk in Psychiatric Disorders'. In this retrospective longitudinal cohort study, we will use different registers connected to the Swedish legal system and other registers. About 800 patients with Schizophrenia, conditions related to Schizophrenia or Affective Disorders that have been treated in different psychiatric clinics in Stockholm since 1973 have participated in different studies in which monoamine metabolites in the CSF were analysed and the results are available in different databases. Those patients who have committed violent crimes will be identified in the National Crime Register kept at the National Council for Crime Prevention. Additionally, patients who had undergone a forensic psychiatric evaluation will be identified in the Forensic Psychiatry Register at the National Board of Forensic Medicine. Patients who have been injured or have died because of victimization will be identified in the National Inpatient Register or the Cause of Death Register kept at the National Board of Health and Welfare. The concentration of monoamine metabolites in patients who had committed violent crimes or have been victimized will be compared with those of patients who had not committed violent crimes or been victims of violent crime.

There is a general paucity of studies on biological risk factors for violence in adult psychiatric, non-forensic cohorts with Mood Disorder or Schizophrenia spectrum psychosis. The planned study will provide further information on risk factors for violence, illness, suicide and the relationships between these risk factors.

8 ACKNOWLEDGEMENTS

First and foremost, I would like to express my gratitude to all the patients and conscripts who took part in the studies in this thesis. Without their contribution, the studies would not have been performed.

It is a great privilege to have had the opportunity to complete this thesis. There are so many people who have helped me to accomplish this work and to whom I am most grateful. My special thanks go out to all the people who, in some way, have been involved, but whom I have taken for granted or forgotten to thank in this Acknowledgement section or in real life – thank you and forgive me!

To all of them I remember, my warmest thanks go to:

My main supervisor, **Jussi Jokinen,** who, with a forgiving attitude and infinite patience with my scientific failures, took control over the situation when necessary, but, at the same time, encouraged me to be creative and to take my first steps to becoming an independent scientist when I was ready for it. Without his enthusiasm, humility and intellectual capacity, this thesis would not have been written.

My co-supervisor, **Erik Jönsson**, for his expertise and knowledge in the scientific field and for putting it all into a larger context, without missing the details.

My co-supervisor, **Peter Nordström**, who made me curious and then introduced me into the research field and kept a watchful eye on my efforts in his research group.

My co-supervisor, **Marlene Stenbacka**, who, with great skill, dedication, patience and good mood, helped analyse and re-analyse many variables in 49,000 men.

My mentor, **Håkan Götmark,** because he is a very wise and ethical person with both feet on the ground who supported me with excellent general, sensible advice.

My co-authors, **Kaj Forslund**, **Marianne Kristiansson**, **Anders Romelsjö**, **Anders Tengström** and **Marie Åsberg,** for absolutely necessary and essential contributions to the studies in this thesis.

My research colleagues, **Peter Asellus**, **Marie Bendix**, **Philip Brenner**, **Andreas Chatzitoffis**, **Josef Isung**, **Mia Rajalin**, **Cave Sinai** and **Jón Hallur Stefánsson**, who increased my knowledge and insights through interesting discussions in Journal clubs and Research seminars under pleasant conditions.

All my bosses in recent years, **Pelle Granström**, **Marianne Kristiansson**, **Maria Carlén-Lindwall**, **Johan Franck** and **Gun Adnell**, who enabled my research through good scheduling and financial support.

I would also like to thank:

All my colleagues at The National Board of Forensic Medicine, The Psychiatry Centre Södertälje and The Addiction Centre Stockholm that covered for me during my absence from the workplaces because of my research during recent years.

My former colleague, **Joakim Sturup,** at The National Board of Forensic Medicine, for interesting discussions when planning a study that has not yet started.

Director of Doctoral Studies, **Robert Harris,** and Education Administrator **Eva Holmgaard** for organization of the educational and administrative support at Karolinska Institutet.

All the teachers and students at the National Research School for Clinicians in Psychiatry in Stockholm and Uppsala, for all teaching and interesting group work and discussions.

The security guards and the police that stopped the hooligans who, at close range, gave me an insight into premeditated violence, and the psychiatric nurses who, on many occasions, prevented impulsive violence in the clinical setting.

All the coaches and friends of the football team Hammarby IF P 05:3, **Jörgen Stattin**, **Anders Sjörin** and **Thomas Pall**, who covered for my absence during training sessions and matches when I was writing this thesis.

My friend, **Urban Konradsson Botes,** for his in-depth analysis of the violence in the movie 'Black Hawk Down' and how it affects us.

All my friends, acquaintances and relatives, for your support.

My parents, **Margareta** and **Martin Moberg,** for encouraging me to pursue my dreams, and my brother, **Magnus Moberg,** for showing me that aggressiveness is best practiced in mutual consent under controlled conditions in a hockey rink and likewise.

Finally, my greatest gratitude goes out to the most important persons in my life: the love of my heart and dear wife, **Cecilia Moberg**, she is the best, and our beloved children, **Josefin**, **Johannes**, **Daniel** and **August**. Thank you for just being who you are and reminding me of things that are more important than science.

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